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Original Communications

URINARY TRACT INJURIES IN OBSTETRICS AND GYNECOLOGY

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SERIOUS damage to the urinary tract during pelvic surgery is a critical misadventure. The exact incidence of occurrence of accidental injury to the lower urinary tract in obstetrics and gynecology is difficult to determine, but it is obvious that these injuries are all too frequent. In spite of the greatest care and skill, severance or occlusion of the ureter and fistula formation have always occurred and probably always will. The increasing employment of the Wertheim radical abdominal panhysterectomy and total vaginal hysterectomy has popularized more daring surgery. We believe that, if this trend continues, it is likely that more, rather than fewer, urinary tract injuries will occur in the future. When major injury is not recognized, death of the patient often ensues.

The technical repair of urinary defects sustained during gynecological surgery seems commonplace to the urologist, but anastomotic procedures are not well understood by the average pelvic surgeon. Successful surgery is simple surgery. Conversely, unsuccessful surgery is complicated. The repair of urinary tract injuries is frequently unnecessarily complicated.

Often more is learned from our mistakes than from our successes. With this thought, then, we have considered certain of our errors and difficulties in this review of urinary tract injuries treated at the University of California Hospital during a recent fifteen-year period. It seems proper to: (1) note the incidence of urinary damage in pelvic surgery; (2) appraise the causes for this

urological damage; (3) suggest means for the avoidance of such accidents; (4) offer methods for the recognition of urological injuries; and (5) present certain operative procedures to be done by the obstetrician-gynecologist for the early correction of urinary tract damage. The most significant results of this study have been the stimulation of interest in pelvic anatomy, operative technique, and certain urological principles vital to the management of urinary tract injuries.

Sixty-two instances of major injury to the urethra, bladder, or ureter, in 49 different women, are presented (Table I). These cases represent our experience during the fifteen-year period, 1938 to 1952, inclusive. During these years, 6,211 major surgical operations (including 458 cesarean sections) were done. One hundred thirty-seven radical Wertheim panhysterectomies are included in this number. Approximately two-thirds of these major operations were abdominal procedures, and about one-half of the hysterectomies done in this fifteen-year interval were total hysterectomies. The incidence of urinary tract injury in this series is 0.83 per cent. Although 11 patients were originally operated upon elsewhere, the final management of all women was finally undertaken by members of the staff of the Department of Obstetrics and Gynecology and/or by consultants from Urology. Ward and private patients are included. The operators who performed the original surgery at our institution where accidents involving the urinary tract occurred were certified obstetrician-gynecologists or were senior residents in training. We have eliminated all cases where urinary tract injury occurred in cystoscopy, and in general or traumatic surgery. We have not considered damage to the urethra, bladder, or ureter by malignant disease, save where definitive pelvic surgery was employed for the elimination of cancer.

Out of a total of 62 injuries, there were 36 instances of damage to the ureter and 25 cases of bladder injury. There was but one accident involving the urethra.

TABLE I. URINARY TRACT INJURIES, 1938-1952

OPERATION TO WHICH ACCIDENTS WERE SECONDARY	URETER	BLADDER	URETHRA	TOTAL
Wertheim radical hysterectomy	20 (1)*	5		25 (1)
Total hysterectomy (other)	7 (3)	3 (3)		10 (6)
Anterior colporrhaphy	3 (1)	5	1	9 (1)
Subtotal hysterectomy	2 (1)	4		6 (1)
Excision of cervical stump	2	2		4
Excision of ovarian cyst	2	1		3
Dilatation and curettage		2 (1)		2 (1)
Cesarean section		2		2
Excision of bladder tumor		1 (1)		1 (1)
Total	36 (6)	25 (5)	1	62 (11)

*Numbers in parentheses indicate injuries which occurred elsewhere.

Ureteral Injuries

Our experience and that of others emphasizes Bland's[1] statement that, "In spite of the prevailing belief that ureteral injury is rare, I believe it to be one of the most, if not the most, frequent as well as the most serious accident of pelvic surgery." The types of injury and the surgical procedures from which they resulted are shown in Table II.

Thirty-six ureteral injuries were recorded in 28 patients. Some of these women also sustained bladder injuries.

It was noted that marked stricture of the ureter (of sufficient degree to cause hydronephrosis) was the most common result of operative injury in gynecological surgery. Thirteen of 36 injuries were strictures and, in 4 cases, the ureter was completely occluded.

There were 9 ureterovaginal and one ureterocutaneous fistulas and 9 proved severed ureters in this series (Figs. 1, 2, 3). All of the cut ureters were recognized at operation. It is probable that several instances of ureteral division are included with the ureteral fistulas, although the fact that most of the fistulas did not appear until after the first week suggests other factors.

The major cause or reasons for the urinary tract damage were apparent in each of the 28 cases. Admittedly, several factors probably played a role. Moreover, other reviewers may correlate certain of these causes differently. In our opinion, however, it appears that complicated surgery, with difficult dissection, was associated with ureteral damage in 13 (46 per cent) of the patients. This represented the largest group of ureteral injuries. Faulty technique was responsible for nine (32 per cent) of the cases. Poor exposure, making dissection awkward, occurred in five (18 per cent) of the cases. Anomalous ureters were met and damaged in one case (4 per cent).

TABLE II. URETERAL INJURIES, 1938-1952

ORIGINAL SURGERY (32 PATIENTS)	URETERAL STRICTURE	URETERAL SEVERANCE	URETERAL FISTULA	URETERAL OCCLUSION	TOTAL
Wertheim radical hysterectomy	8	4	7 (1)*	1	20 (1)
Total hysterectomy (other)	3	1 (1)	3 (2)		7 (3)
Anterior colporrhaphy	1 (1)			2	3 (1)
Subtotal hysterectomy		1		1 (1)	2 (1)
Excision of cervical stump	1	1			2
Excision of ovarian cyst		2			2
Total	13 (1)	9 (1)	10 (3)	4 (1)	36 (6)

*Numbers in parentheses indicate injuries which occurred elsewhere.

Avoidance of Ureteral Injury.—

The avoidance of urinary tract damage is, of course, more important than the methods of repair, if we believe that "an ounce of prevention is worth a pound of cure." Preoperative urological study and preparation of the patient are most important where cancer, tumor, endometriosis, or infection involves the pelvic structures. The patient who presents such pathology should be admitted to the hospital several days prior to operation and tests of urinary function obtained. These should include a phenolsulfonphthalein determination, a dilution-concentration test, and intravenous pyelography. If incompetency or distortion of the urinary tract is discovered, further studies involving cystoscopy, retrograde pyelography, and including individual kidney function tests will be required.

Insertion of ureteral catheters preliminary to difficult pelvic surgery has generally been considered good practice. Brown[2] stated, however, that it is occasionally impossible to locate the ureter by palpation even with a catheter in situ. Latzko and Schiffmann[3] insist that, in most cases, preoperative ureteral catheterization is superfluous and not entirely free from danger. They believe that inlying ureteral catheters should not be employed as a routine. Current urological thinking, however, favors the insertion of adequately placed, sizable x-ray ureteral catheters before surgery. The main deterrents to preoperative catheterization seem to be reluctance on the part of the surgeon to call a cystoscopist for consultation, the added cost, and the brief delay in effecting the necessary surgery. A catheter will facilitate ureteral repair, if this is required, however. It will also represent an inlying splint, as well as

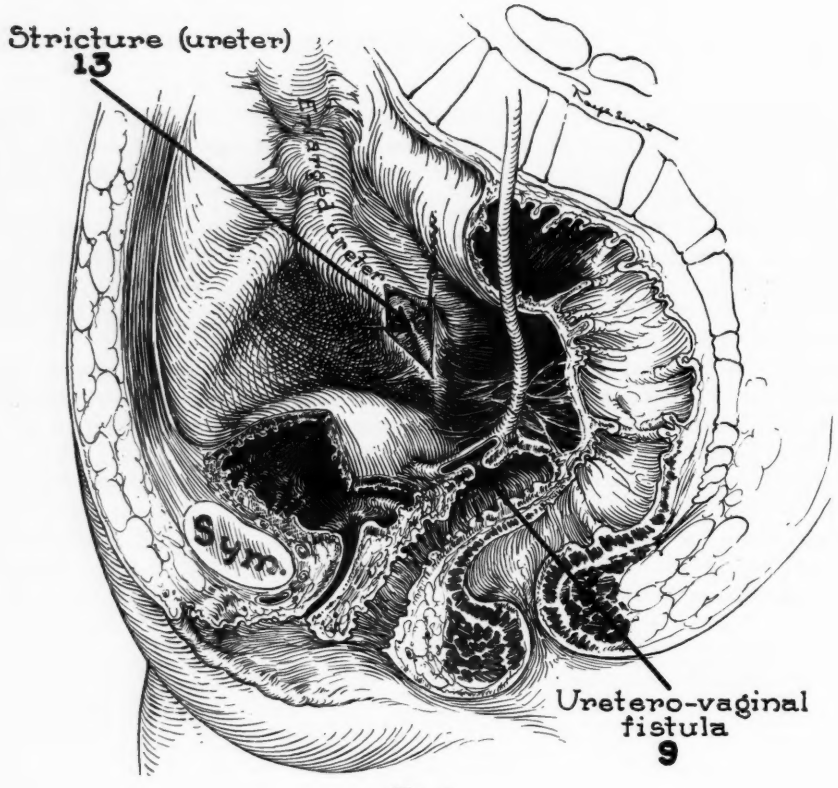

Fig. 1.

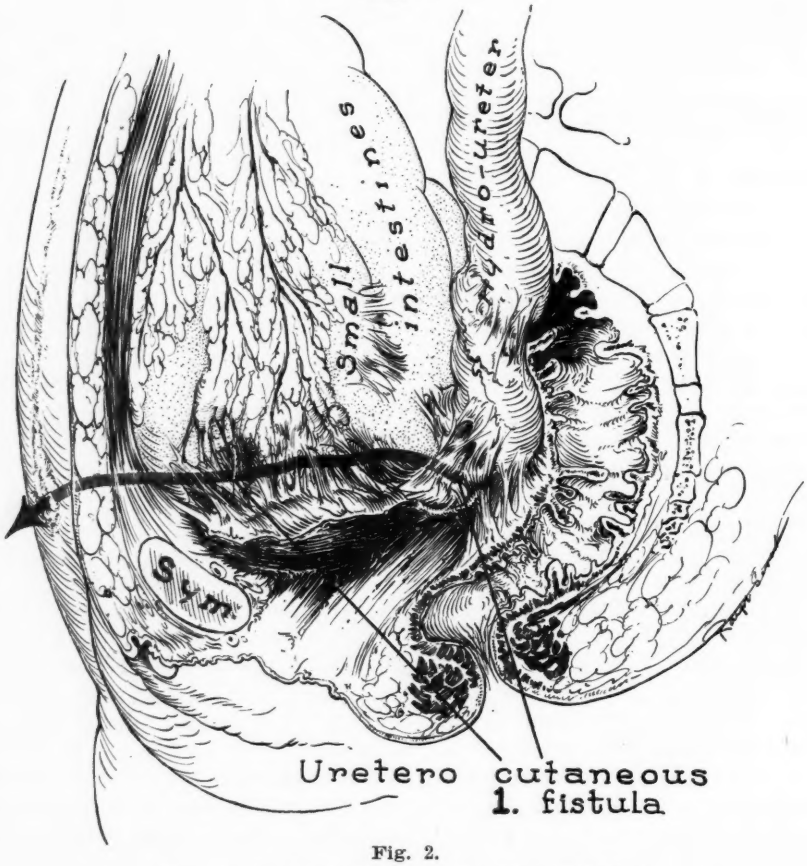

Fig. 2.

Figs. 1, 2, and 3.—Ureteral injuries sustained.

a drain, in cases where trauma, kinking, or partial suture obstruction to the ureter occurs. The rare occurrence of ureteral damage in our patients who were properly prepared and in whom ureteral catheters were placed attests to the value of anticipating catastrophe.

Incomplete mobilization of the bladder from the cervix in total hysterectomy, done vaginally or abdominally, invites accident by retaining the ureter too close to the field of clamps and ligatures. Adequate dissection of the bladder off the cervix may be particularly difficult when previous surgery or irradiation has been effected. Sharp dissection is often necessary, and time-consuming meticulous surgery may prevent serious bladder or ureteral injury.

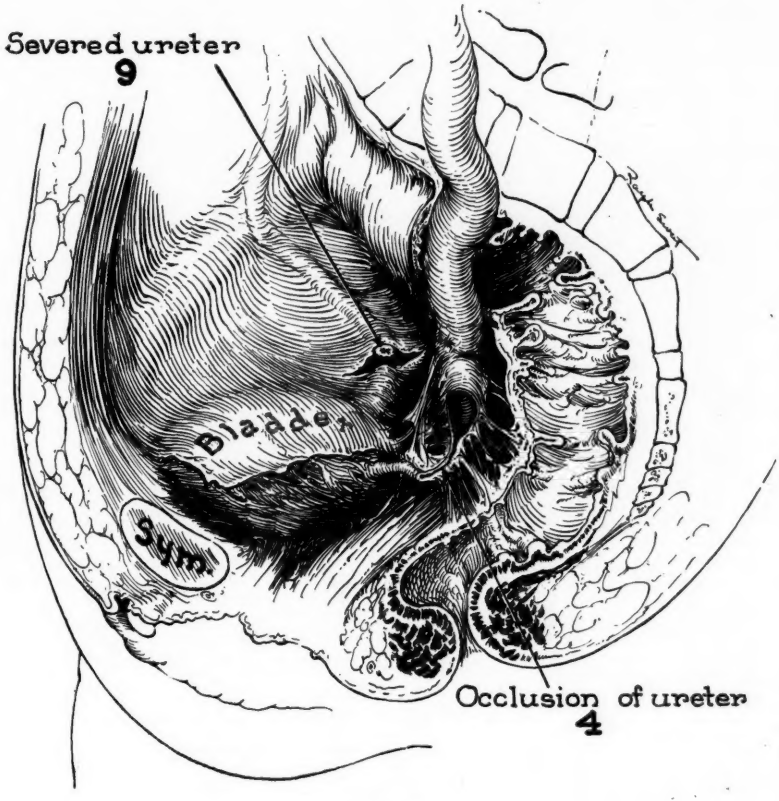

Fig. 3.

It has been emphasized that one should never tie vessels of the lower uterine segment unless the peritoneum has been turned out. In a Wertheim total hysterectomy, one should leave the ureter attached to the peritoneum laterally in its upper portion and medially in its lower portion.[4] Vaginal closure by preliminary development of the pubocervical fascia, as described by Richardson[5] and also by Judd,[6] reduces the likelihood of ureteral and bladder injury.

Four danger zones have been described where injury to the ureter may occur. The *first,* but least dangerous, is the point where the ureter crosses the iliac vessels. The *second* is the ovarian fossa where the ureter comes in close proximity to the adnexa, so long as the ovary and tube remain in normal position. The *third,* and most serious point where damage is likely, is the ureteral slit where the ureter is crossed by the uterine vessels. Scarring or

TABLE III. DEATHS FROM URINARY TRACT INJURIES IN OBSTETRICAL AND GYNECOLOGICAL SURGERY, 1938-1954

U. C. H. NO.	URINARY LESION	OPERATION TO WHICH INJURY WAS SECONDARY	LESION FIRST NOTED	MEANS OF CORRECTION	RESULT	CAUSE OF GENITOURINARY DAMAGE	REMARKS
121098	Laceration bladder extensive	Subtotal abdominal hysteromyomectomy	At operation	Closure	Death, eleventh postoperative day	Poor exposure. Large myoma	Catheter drainage but extravasation, infection. Pulmonary embolus
121408	Laceration bladder	Manchester operation, third-degree prolapse	Third postoperative day	Inconclusive cystoscopy, third postoperative day, tidal drainage (no laparotomy)	Death, eighth postoperative day	Faulty technique. Poor exposure. Laceration unrecognized	Extravasation of urine. Infection, pneumonia. Death from sepsis
123487	Occlusion ureter, left	Pelvic lymphadenectomy for carcinoma of cervix	At operation	None possible. Hemorrhge	Death, seventh postoperative day	Hemorrhage. Deliberate mass clamp compression	Death from hemorrhage, ileus

TABLE IV. TREATMENT OF URETERAL INJURY

1. Deligation
2. Anastomosis (first, establish drainge, then, re-establish continuity, and splint)
   a. Ureteroureteral anastomosis
   b. Ureterovesical anastomosis
   c. Ureterointestinal anastomosis
3. Decompression
   a. Tube ureterostomy
   b. Nephrostomy
4. Purposeful ligation of ureter
5. No treatment but drain; nephrectomy

distortion may occur here. A *fourth* danger point is at the base of the bladder, where incisional damage or kinking of the ureter can occur. At this last point, traction extending into the interureteric ligament may obstruct the ureter. This is particularly likely during attempts at vaginal closure of vesiocovaginal fistulas.[7]

Damage to the ureter may result from reduction of its blood supply during dissection, for example, when the ureter is elevated, as in the Wertheim operation. According to Anson,[8] the ureter enters the lesser pelvis by passing over the point of division of the common iliac artery where it divides into the external iliac and hypogastric. Here, the ureter lies just above the hypogastric artery and receives a branch of its blood supply from this vessel via ascending and descending rami. The inferior vesical, a branch of either the uterine or the hypogastric artery, supplies the lower portion of the ureter, as do branches of the inferior hemorrhoidal artery. The superior vesical artery serves the ureterovesical juncture. In radical panhysterectomy, ligation or damage to these vessels endangers the ureter.

The peritoneum overlying the ureter, particularly in the lower portion, also supplies the ureter with small vessels. It must be recalled that the blood supply of the ureter is largely in the adventitia, so that wide stripping of the duct from the peritoneum and its bed may endanger ureteral nutrition. Careful preservation of the ureteral blood supply and avoidance of gross denudation of this structure will avoid delayed necrosis and fistula formation.

AVOIDANCE OF URETERAL DAMAGE

1. Do not operate without adequate preliminary studies of the urinary tract and knowledge of the anatomy and pathology involved.
2. Catheterize and recognize the ureter initially in all difficult cases.
3. Identify all structures before clamping, incision, and ligation.
4. Avoid undue traction and needless denudation of the ureter and base of the bladder.
5. Employ deft technique with fine absorbable suture material in or about the urinary tract.
6. Be careful and resourceful, and apply pressure, not mass ligature, for hemorrhage; then secure the bleeding point.
7. Splint the ureter, drain the bladder, and drain the wound cavity (extraperitoneally) in suspected urinary tract injury.
8. Order ample and well-chosen chemotherapy in complicated cases.

In pelvic surgery, the grave fault lies not so much in the injury of the ureter (or bladder), but in the failure to recognize this damage. The most important consideration is the provision for adequate drainage of the kidney, whether by properly executed reanastomosis or by diversion of the urinary stream. The dangers of unrecognized ureteral damage lie in extravasation of infected urine. This will finally lead to irreversible pathological changes.

After major abdominal surgery, the course of the ureter should be traced, beginning at a point well above the operative area and extending to the insertion of the ureter into the bladder. The fact that the ureter contracts actively aids in its identification. If there is still doubt as to its integrity, indigo carmine or dilute methylene blue can be injected into the proximal ureter to note extravasation or obstruction. An alternative method is to place two fine stay sutures in the ureter and through a small incision between them insert a No. 5 or 6 F. ureteral catheter toward the bladder. If a ureteral catheter has been placed prior to surgery, the surgeon himself should withdraw it to detect any undue "hang" suggestive of ligation.

A study of the 3 deaths in this series indicates that if prompt recognition, preferably at operation, had been achieved in the 2 instances of bladder injury (Table III), extravasation of urine, leading to infection and death, might have been avoided. Breach of the principles of adequate exposure and proper technique in the management of urological injury were basically responsible for these deaths. Laceration of a major vessel during radical surgery may require heroic measures, such as mass ligature, but only with danger to the urinary tract.

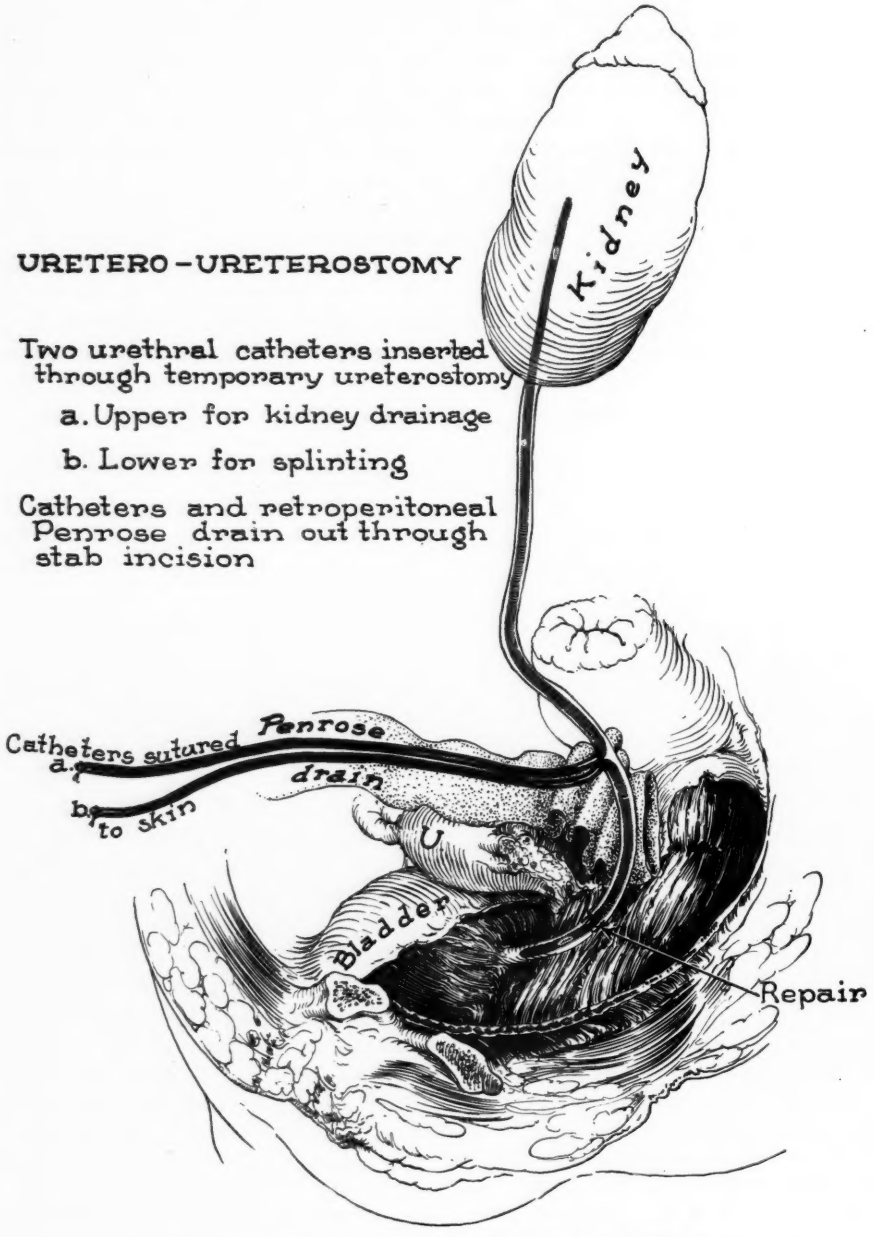

Fig. 4.—Ureteroureterostomy (with two catheters).

Treatment of Ureteral Injury.—

If the accident is *recognized at the time of the initial operation,* treatment is greatly simplified. Three basic urological principles which may be overlooked must be observed for safety and for good results. First, adequate drainage must be provided for possible leakage of urine, whether a watertight repair can be done or not. Second, continuity of the urinary conduits should be attempted, since proper coaptation will decrease leakage and peri-

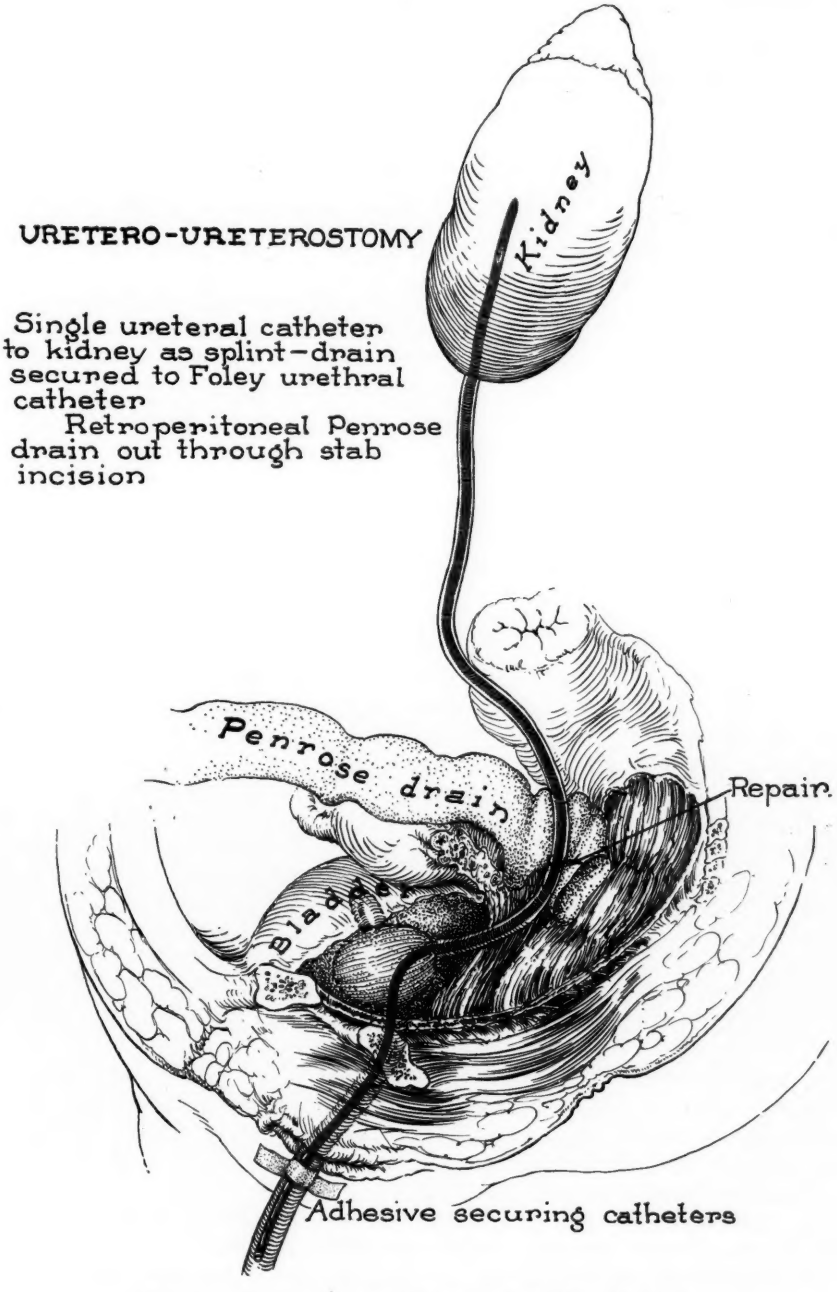

Fig. 5.—Ureteroureterostomy (with single catheter).

TABLE V. INVESTIGATION OF POSTOPERATIVE ANURIA

ureteritis, and allow proper peristaltic flow. Third, the area of repair should be splinted with an indwelling tube, to permit epithelization and decrease scarring, with later contracture and obstruction.

With these basic concepts in mind, certain operative procedures which apply to most cases will be reviewed (Table IV).

Deligation is indicated if mass ligatures have encircled the ureter, as proved by obstruction to a catheter passed from above. After deligation, one must make certain that necrosis or perforation of the ureter has not also taken place.

Anastomosis is most often required when the injury is detected at the operating table, since severance of the ureter is more often noticed than ligation.

Reanastomosis of the proximal ureter to the ureteral stump (ureteroureterostomy) (Figs. 4 and 5) is the procedure of choice since it does not require pulling the ureter down and does not require opening of the bladder. A T-tube technique is recommended.[9] Stay sutures are placed through both cut ends, so that they can be manipulated without grasping forceps. A T-tube is notched at the T. A short incision is then made 2 to 4 cm. above the site for anastomosis, and the lower arm of the T-tube inserted through it to traverse the anastomotic site into the distal segment. The upper arm is passed proximally. Four No. 4-0 chromic everting mattress sutures close the defect around the tube as a splint. It is most important to make a stab incision in the lower abdominal quadrant and dissect extraperitoneally to the site of anastomosis, so as to lead the long arm of the T-tube and a Penrose drain out of the body without traversing the peritoneal cavity.

Alternatively, if the distal stump is too short, anastomosis of the ureter to the bladder (ureterocystostomy) (Fig. 6) is indicated. The bladder is adequately opened extraperitoneally, and an oblique stab incision is made in the posterior wall, close to the trigone on the damaged side. The ureter, after its end has been split (fishmouth fashion), is drawn through the bladder incision and fixed by catgut sutures which pass through all thicknesses of the bladder. Using another method, the end of the ureter may merely be cut obliquely and anastomosed, mucosa to mucosa, to the bladder wall. In either case, additional tacking sutures are desirable on the exterior of the bladder. This anastomosis may or may not require splinting. The best splint is a T-tube inserted through a small incision in the ureter, with the lower arm extending into the bladder and the long arm running extraperitoneally to the body wall. Another satisfactory method is the use of small *urethral* catheters through a short incision in the ureter, one running up to the kidney pelvis, and the other running down into the bladder and brought out extraperitoneally. Urethral catheters are preferable because of their flexibility and longer lumina. Or, less desirable, a ureteral catheter can be passed from the bladder to the renal pelvis, and the other end passed through the urethra and attached to a balloon catheter. In either case, extraperitoneal drainage must be provided.

If the ureter has been so badly damaged that neither of these methods is possible, the surgeon might consider anastomosis of the ureter to the large bowel (ureterosigmoidostomy) (Fig. 7). The complications of this procedure (obstruction and chronic infection) so commonly follow even elective ureterocolic anastomoses, however, that we would rather recommend a simple drainage procedure such as tube ureterostomy (Fig. 8). This would allow the patient to recover so that contralateral renal function can be evaluated, and a decision made between nephrectomy or the use of a segment of ileum to bridge the gap.

Decompression is indicated if there is not time for a careful, skillful anastomosis. It is greatly preferred to a poorly done implantation into the bladder or especially into the bowel. One can gain time by simply placing a small urethral catheter (No. 10 or 12 F.) up the ureter from the cut segment and passing the butt end extraperitoneally through a stab wound in the lower abdominal quadrant.[10] The patient will recover from her operation, and the other kidney can be evaluated. Then, at some later time, with ureterograms

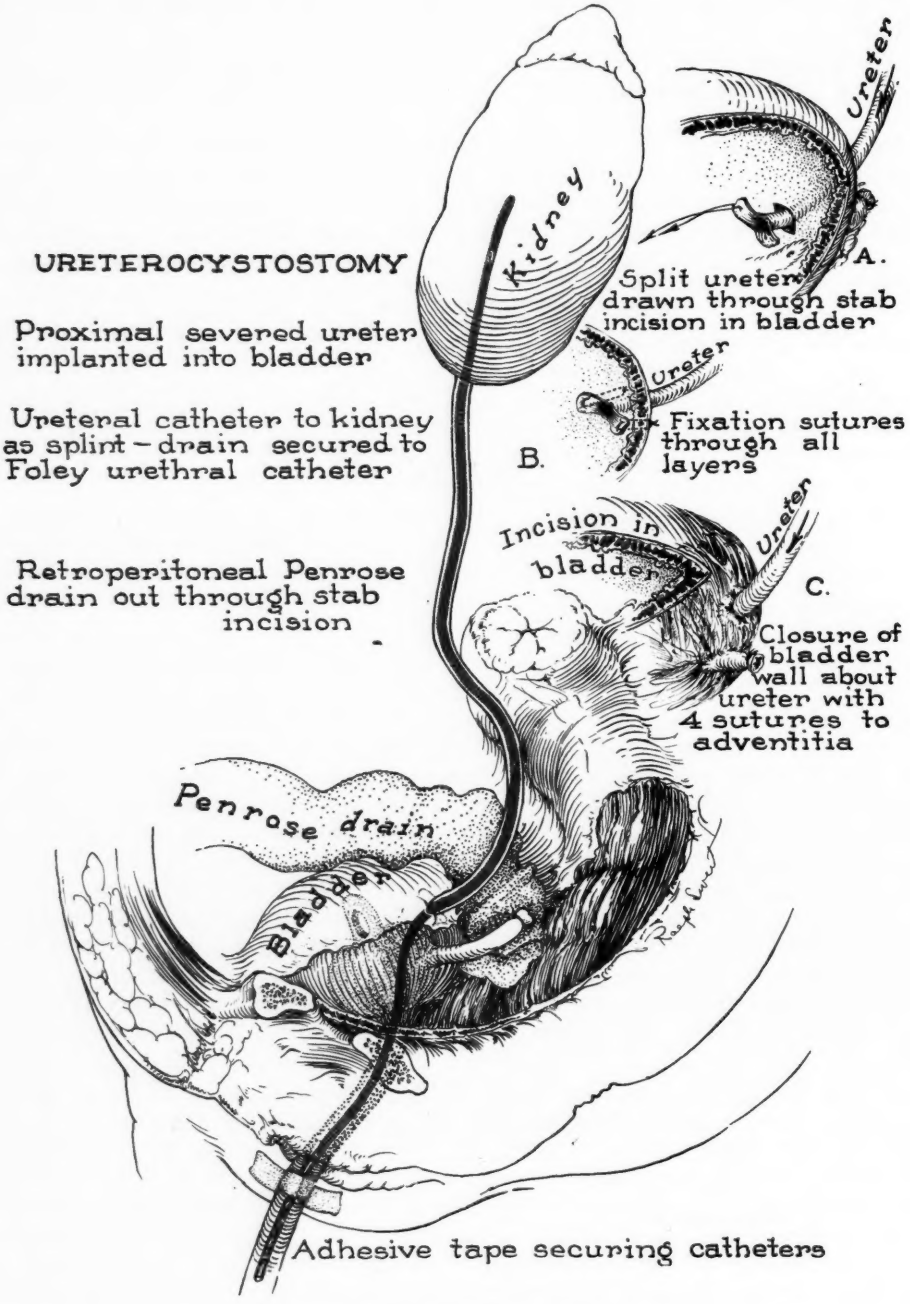

Fig. 6.—Ureterocystostomy (technique).

as a guide, definitive repair can be planned. Antegrade pyelograms[11] are helpful in outlining the condition of the injured ureter.

Purposeful ligation of the ureter is not a procedure of choice for the good reason that a surgeon cannot be certain that the contralateral kidney is, and always will be, normal and free of disease. In addition, ligation is not always followed by simple hydronephrotic atrophy of the kidney. Infection may follow, or leakage with subsequent ureterovaginal or ureterocutaneous fistula. If ligation is done, however, nonabsorbable suture material is used.

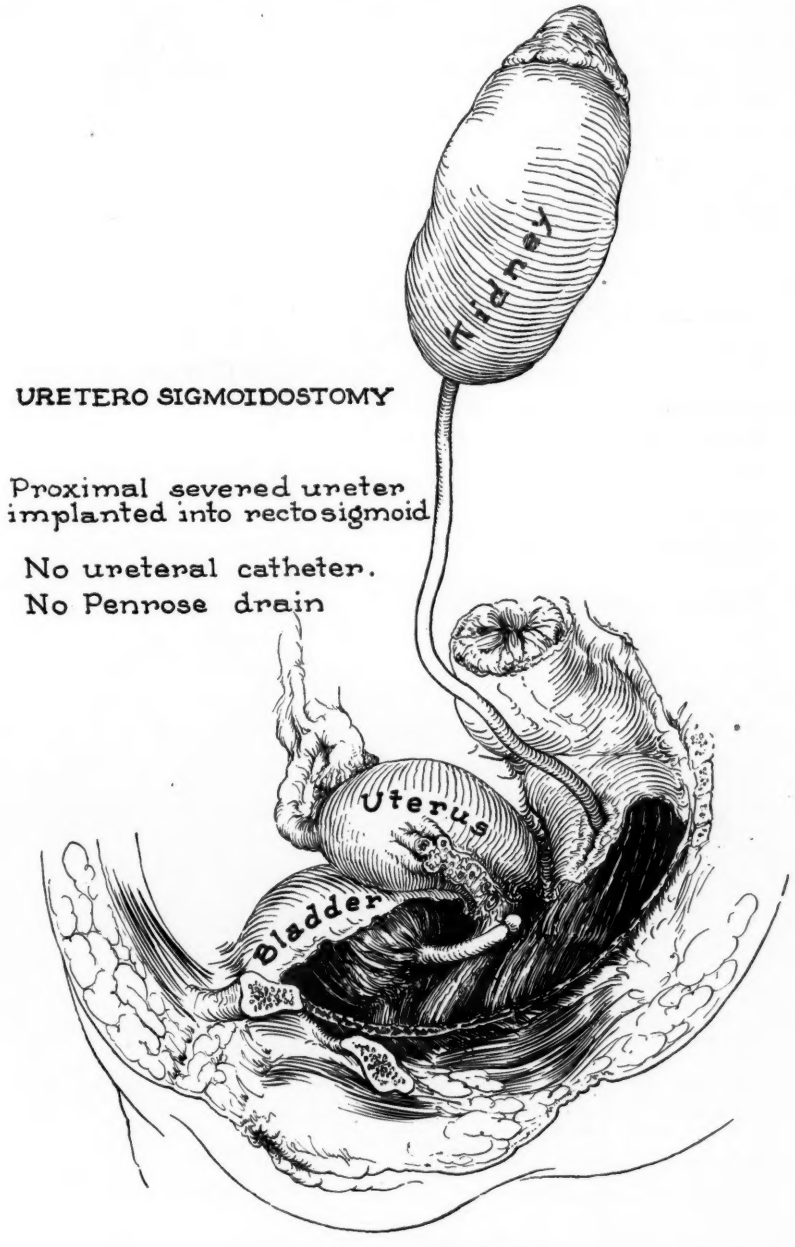

Fig. 7.—Ureterosigmoidostomy.

If the injury is not recognized at the time of the surgery, considerable judgment is required in choosing the best time for repair and the best method for accomplishing it.

Anuria usually is caused by factors other than bilateral ureteral ligation. Table V is presented as a guide to differentiation. The phenolsulfonphthalein test (PSP) will distinguish real renal damage (lower nephron nephrosis or bilateral ureteral occlusion) from prerenal oliguria, caused by dehydration or even cardiac failure. A very low or absent PSP excretion after a gyne-

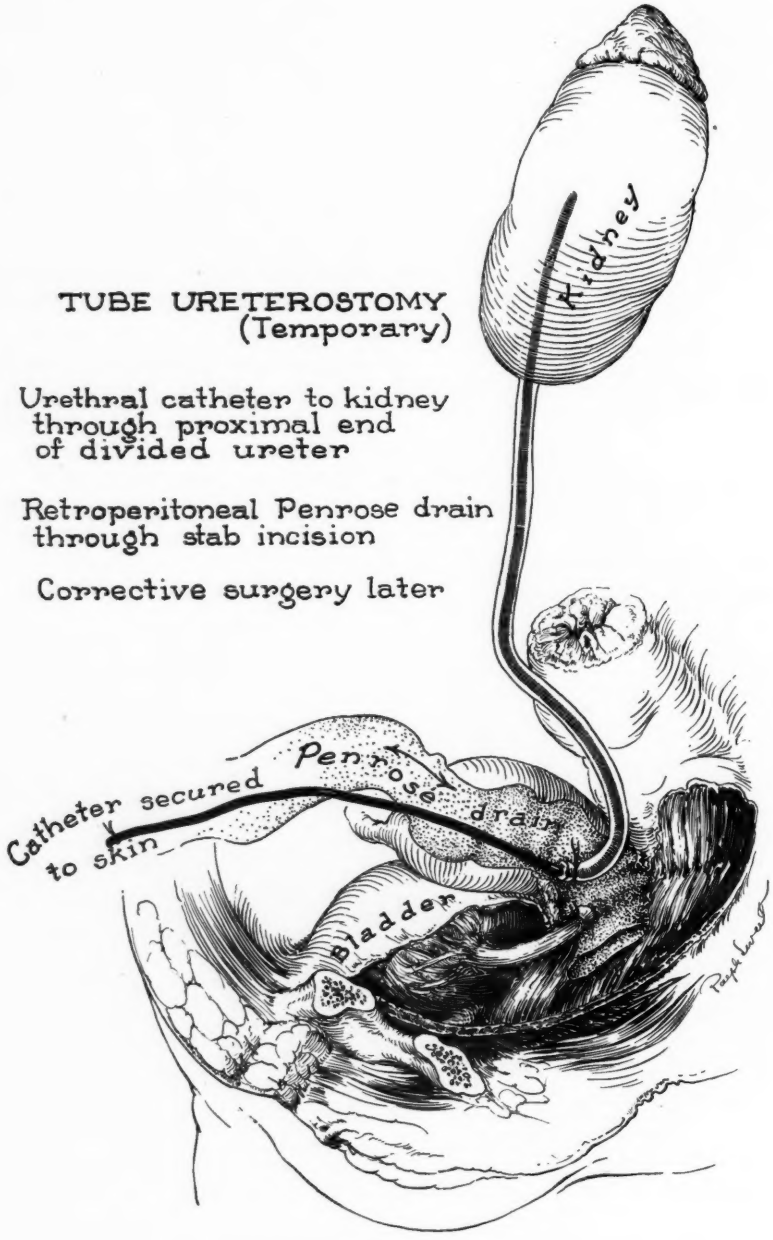

Fig. 8.—Tube ureterostomy.

cological operation in which sutures or dissection approached the ureters is indication for prompt ureteral catheterization. If the catheters pass easily to both renal pelves and urinary flow is not obtained, renal oliguria-anuria is present. A retrograde pyelogram, using small amounts of dye, will rule out extravasation, if this is suspected.

If the catheters are blocked in the ureters, the exact site of the obstruction will be determined thereby. Dye is injected through the catheters and an x-ray film exposed, allowing estimation of the degree of obstruction.

Deligation should be attempted only if the patient is in good condition. Often, accidental ligation is found only when the patient fails to excrete urine; by that time she is in poor general condition. In that case, nephrostomy, or even tube ureterostomy, would be preferable to deligation, because these procedures would guarantee adequate renal drainage, which the deligation would not. Also, if deligation fails, the secondary repair will be more difficult because of the added dissection.

Anastomosis is done by techniques similar to those outlined above. Nevertheless, the surgeon should not be forced by the patient to intercede too soon—many ureterovaginal fistulas heal spontaneously.

Decompression, as we have indicated, is often lifesaving. A nephrostomy will make later repair easier.

Nephrectomy is desirable in older patients with damage to the kidney from infection associated with fistula. It may be required after previous failures to repair the defect. Nephrectomy should be done, of course, only after study shows the other kidney to be normal.

Bladder Injuries

Twenty-five bladder injuries in 25 patients are considered in the present series. We have divided the accidents into the following categories: (1) bladder incision or laceration, (2) vesicovaginal fistula, and (3) vesicoabdominal fistula, as shown in Table VI (Figs. 9, 10).

Avoidance of Bladder Injury.—

In ascribing the cause for these difficulties, it appears that 8 of the bladder incisions or lacerations were due to scarred tissues, generally the result of previous surgery and/or radiation, with complicated dissection. Five vesicovaginal fistulas were considered also to be due to difficult surgery. Four of the bladder lacerations were the result of faulty technique, as were 4 instances of vesicovaginal fistula, and one vesicoabdominal fistula. Poor exposure was the principal reason for three lacerations of the bladder.

Our experience indicates that Feeney[12] is correct in stating that bladder injuries in *abdominal* surgery may occur in the following situations and particular care should be taken to avoid them:

1. During incision into the parietal peritoneum. (Incompletely emptied bladder. Adhesions from previous surgery. Displacement of the bladder by tumor.)
2. With downward displacement of the bladder during total hysterectomy. (Skeletonization and ligature of uterine vessels. Severance of lateral cervical attachments.)
3. At the time of dissection for removal of the cervical stump or intraligamentous tumor, or in sling, "pin-up" operations for urinary stress incontinence.
4. In cesarean section, particularly extraperitoneal, when the bladder is dissected free of the anterior uterine segment.

Bladder injuries in *vaginal* surgery may occur:

1. At the division of the anterior vesical ligament and the so-called pillars of the bladder.
2. In exposure of the lateral ligaments of the cervix during vaginal hysterectomy or the Manchester operation.
3. During dissection for access to the anterior cul-de-sac during interposition operations or vaginal hysterectomy.
4. In anterior colporrhaphy when the distal end of the posterior urethral ligament is secured to the anterior cervix.

Infection, hematoma, deep sutures, and overdistention of the bladder may be secondary causes for bladder injury and fistulas.

Treatment of Bladder Injury.—

The repair of bladder injuries requires their prompt recognition. The use of sterile, canned, evaporated milk, or dilute methylene blue may serve to demonstrate a bladder defect at surgery. An indwelling catheter, without tidal drainage, for at least ten days is proper procedure where bladder damage is noted and repaired. If a bladder fault is unrecognized and extravasation of urine occurs, cystoscopy is rarely helpful and is usually inconclusive. A cystogram is by far the best procedure to note extravasation. Occasionally, the passage of ureteral catheters may be required to differentiate the leakage from that of a ureterovaginal fistula. Secondary surgery for the closure of a damaged bladder may dispel a crisis, and perhaps a fatal termination.

TABLE VI. BLADDER AND URETHRAL INJURIES, 1938-1952

ORIGINAL SURGERY (25 PATIENTS)	BLADDER INCISION OR LACERATION	VESICOVAGINAL FISTULA	VESICOABDOMINAL FISTULA	TOTAL
Wertheim radical hysterectomy	3	2		5
Total hysterectomy (other)	1 (1)*	2 (1)		2 (2)
Anterior colporrhaphy	4	1		5
Subtotal hysterectomy	3	1		4
Excision of cervical stump	1	1		2
Excision of ovarian cyst	1			1
Dilatation and curettage		1 (1)	1 (1)	3 (2)
Cesarean section	2			2
Excision of bladder tumor		1 (1)		1 (1)
Total	15 (1)	9 (3)	1 (1)	25 (5)

*Numbers in parentheses indicate injuries which occurred elsewhere.

In about half of our cases of bladder injury, the problem was recognized at operation and a repair effected. Fistula formation was not uncommon, however, and leakage of urine was then recognized between the second and third postoperative weeks.

Two urological principles must be kept in mind when the surgeon is faced with a bladder injury. First, the site of repair must be adequately drained, extraperitoneally. Second, the bladder itself must be drained, so that urine cannot accumulate.

The actual closure of a fresh wound in the bladder is simple. Sufficient bladder wall is mobilized to allow closure without tension. The submucosa (preferably without the mucosa) is closed with fine catgut sutures. Nonabsorbable material is never used near the urinary tract, because it will cause a fistula to persist and may be the nidus for a stone. The muscularis and adventitia are closed in one layer with No. 0 chromic catgut, and then the peritoneum overlying the damaged area is approximated. A Penrose drain is inserted to the area and led out extraperitoneally.

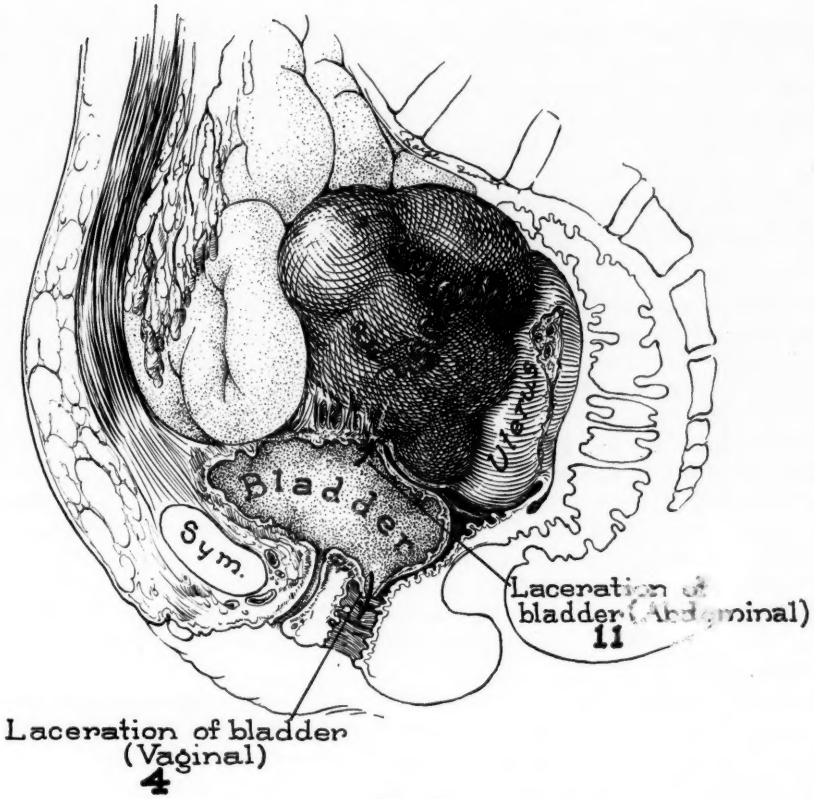

Fig. 9.

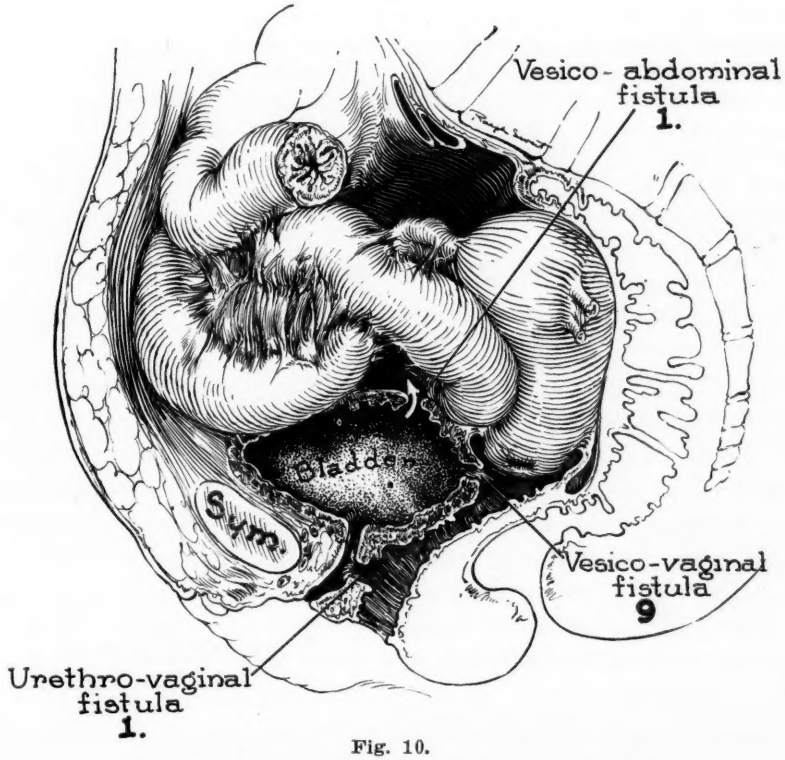

Fig. 10.

Figs. 9 and 10.——Bladder and ureteral injuries.

The bladder itself is usually adequately drained by an inlying urethral catheter. If the damage is extensive, or if breakdown is possible, a cystostomy tube should be placed either vaginally or suprapubically.

Although our series is small, it appears that laceration or incision of the bladder, if discovered at operation and repaired properly, has an excellent likelihood of healing without complications. Vesicovaginal fistulas usually heal at secondary operation if closed carefully three or more months after the original operation.

Urethral Injuries

Damage to the urethra in obstetrics generally follows a long labor, with impaction of the presenting part beneath the symphysis for a protracted period of time. Traumatic vaginal delivery with laceration of the urethra by instruments or spicules of bone, as in craniotomy, may also injure the urethra. With better obstetrics, however, accidents to the urethra and bladder in parturition have become infrequent. In the series reported here, there were no obstetrical urethral injuries.

Urethrovaginal fistulas may follow anterior colporrhaphy. This lesion is likely to occur when previous surgery necessitates sharp dissection beneath the urethra, or when the surgeon boldly incises the vaginal wall for entry into the anterior vaginal cleavage planes. Although we had no such casualties, it is known that faulty repair, infection, hematoma, or inadequate closure following excision of a urethral diverticulum occasionally lead to a persistent urinary defect.

Traumatic catheterization, especially after the repair of urethrocele or relaxed vesical neck, may cause fistula formation. The postoperative catheterization of gynecological patients with rigid catheters or stylet-guided soft catheters should be forbidden. One urethrovaginal fistula, following inept bladder catheterization by a nurse ten days after vaginal repair, is included in our series. A glass catheter was used in this instance.

If urethral injury is recognized at operation, it must be corrected then. Proper mobilization of tissue layers and coaptation with fine interrupted, absorbable sutures is required. Adequate provision for drainage of urine by urethral catheter or by vaginal or suprapubic cystostomy is usually necessary for successful healing. There are few indications, however, for hasty repair of urethral injuries when they are discovered in the postoperative period. Secondary surgery four to six months after the original operation is desirable.

Summary and Conclusions

1. The current trend in pelvic surgery is toward increasingly radical operations. Gynecologists should be able to avoid and to correct the numerous urinary tract injuries which become more likely during complicated or daring operative procedures.

2. A review of fifteen years' experience in the Department of Obstetrics and Gynecology at the University of California Hospital, San Francisco, comprising 36 ureteral injuries, 25 bladder injuries, and one urethral injury, and their repair, indicates that the radical Wertheim, as well as traditional panhysterectomies, were associated with the largest number of ureteral accidents. Bladder damage occurred more frequently after other major surgical procedures, such as anterior colporrhaphy and subtotal hysterectomy.

3. Gynecological surgery involving the removal of malignant or complicated benign proliferative or irradiated lesions greatly endanger the ureter

and the bladder. Inadequate incisions and poor relaxation of the patient during operation handicap the operator in obtaining proper exposure. Ill-advised blunt or, at times, sharp dissection, excessive traction, and poor hemostasis are other faults in technique which encourage urinary tract injury and fistula formation.

4. Urinary reparative and anastomotic procedures are not well understood by the average pelvic surgeon, but are usually successful in the hands of those familiar with the proper, accepted techniques. Most frequently disregarded is provision for adequate urinary drainage from the site of repair. Careful re-establishment of continuity of the urinary conduits and the more frequent use of catheter splints to prevent secondary complications, such as stricture formation, are emphasized.

5. Practical technical details which apply currently employed urological principles for the repair of accidental injury to the urinary tract are described and illustrated.

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LATE RESULTS OF PELVIC SURGERY*

II. Some Results Following Hysterectomy and Pelvic Plastic Procedures

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IN A previous publication,[1] attention was directed to the large number of functional and organic disorders following pelvic surgery among patients who came to our clinic for subsequent care. The patients whose surgery included hysterectomy presented less persistent symptoms, however, than those who had had other types of gynecological surgery.

It seemed, therefore, imperative that we should analyze the results of our personal surgery, in order to attempt to establish reasons for the improved conditions of the patients who had been subjected to hysterectomy. The records from our two local hospitals were examined and all of our major gynecological surgical cases were compared with our follow-up office records. An insignificant number involving emergency surgery for ovarian and tubal pathology were excluded as were cases involving diseases of the vulva. The majority of the cases had been seen by members of our clinic after the initial phase of healing, and therefore all those we subjected to surgery were included for the completeness of the survey. A few had been seen by other gynecologists, urologists, or referring physicians who relayed their outcome to us.

By reference to Table I, it is seen that there were 236 cases involving hysterectomy and 100 vaginal plastic procedures carried out through the five and one-half year period. Of this number, total abdominal hysterectomy, with or without adnexal surgery or repair procedures, constituted 70 per cent of our hysterectomy cases. Vaginal hysterectomy accounted for 24 per cent and subtotal hysterectomy 6 per cent. Of the 236 hysterectomies, 34 had an associated vaginal repair, but only 8 had extensive work including vaginal repair of the anterior vaginal wall. The latter procedure constitutes a time-consuming procedure which adds to the surgical risk, while perineorrhaphy, with or without the Marshall-Marchetti-Krantz procedure, does not add materially to the surgical risk of hysterectomy.

In our previous study, a number of patients who had had abdominal hysterectomy came to our offices because of cystoceles, rectoceles, and shortened vaginas. We therefore attempted to evaluate each case prior to surgery in terms of pelvic support in addition to the more obvious complaints of pain, bleeding, discharge, or other disorders incident to a disease of the uterus. We then added to our hysterectomy technique a repair of the fascial relaxation around the uterus, and repair of the perineum if it seemed indicated at the end of the abdominal or vaginal hysterectomy.

*Presented at the Twenty-sixth Annual Meeting of the Texas Association of Obstetricians and Gynecologists, Houston, Texas, Feb. 26, 1955.

TABLE I. TYPE OF SURGERY AND AGE DISTRIBUTION

OPERATION	TOTAL	AGE 25-30	30-40	40-50	50-60	60 +
Hysterectomy, abdominal, complete		1	25	53	6	3
Hysterectomy, abdominal, complete + adnexa on 1 side			14	9		
Hysterectomy, abdominal, complete + adnexa on both sides			8	12	1	
	132					
Hysterectomy, supravaginal		1	4			
Hysterectomy, supravaginal + adnexa on 1 side			5			
Hysterectomy, supravaginal + adnexa on both sides			2	1		
	13					
Hysterectomy, vaginal + repair			11	17	16	13
	57					
Hysterectomy + anterior-posterior repair			4	4		
Hysterectomy + marchetti + perineal			1	5		
Hysterectomy + perineal			7	13		
	34					
Total	236					
Vaginal repair, anterior-posterior + conization of cervix		5	22	11	6	6
Vaginal repair, anterior-posterior + amputation of cervix		2	4	1	1	
Repair cervix and perineum		6	14	4		
Repair perineum		1	3	2		
Vaginal or abdominal suspension + perineal repair		5	7			
Total repair	100					
Grand total	336					

The majority of the vaginal repair procedures consisted of anterior and posterior vaginal repair with cauterization, conization, or amputation of the cervix. Our technique differed only in that an attempt to support the cervix was made by an incision posterior to the cervix. Through this incision the uterosacral ligaments were shortened, in an attempt to raise the uterus higher into the pelvis. Pelvic exploration was made, if indicated, through the cul-de-sac incision.

TABLE II. INDICATIONS FOR SURGERY

	PELVIC PAIN	ABNORMAL BLEEDING	RELAXATIONS	TUMORS	URINARY DISORDERS	CERVICAL DISORDERS
Total hysterectomy (132)	111	84	20	76*	5	15
Subtotal hysterectomy (13)	11	13	3	9		
Vaginal hysterectomy (57)	40	11	57		12	5
Hysterectomy and vaginal repair (34)	34	20	34	13*	6	6
Vaginal repair (100)	100	24	100		12	55

*13 cases endometriosis.

The age span of these patients is essentially the same, though, of course, more older patients had vaginal hysterectomies, and a younger group the

primary plastic procedures. This reflects a conservative approach in both groups, but for opposing reasons.

Table II attempts a summary of the indications for surgery. It seems significant that pelvic pain and functional bleeding are the most prevalent symptoms and that urinary disorders do not constitute a significant number of problems in our small series. Thirteen cases of endometriosis were found among the 98 "tumors" while adenocarcinoma of the uterus was found incidentally in 3. These "tumors" were primarily myomas or ovarian pathology other than simple follicular cysts. It is obvious that in most of the cases there was more than one indication for surgery and that clinical judgment must enter each problem prior to surgical intervention. This makes a chart of the indications for surgery confusing, but does emphasize the outstanding indications. There were many minor relaxations of the pelvic ligaments among the hysterectomy group and decisions were necessary regarding whether to do a vaginal hysterectomy, do repair work in addition to the abdominal hysterectomy, or rely on the repair of the endopelvic fascia through the abdomen to take care of these disorders. This analysis was prompted by our impression that good vaginal support followed a carefully done abdominal hysterectomy without the necessity of added work on the anterior vaginal wall or on the frequently seen rectoceles.

TABLE III. DISORDERS REMAINING AFTER ONE OR MORE YEARS

	HYST. TOTAL	HYST. SUBTOTAL	HYST. VAGINAL	HYST. + REPAIR	VAGINAL REPAIR
Ovarian pain or disease			2		10
Uterine pain or disease					15
Urethral disorders	6		12	3	5
Cystocele	2				2
Rectocele	4	1	2		
Cervical disease		2			10
Dyspareunia	1		2		6
Anxiety					4
Menopause	4	1		3	4
Asthenia			2		4
Headache					3
Obesity	9	1	3		3
Per cent symptomatic	19	16	29	17	48

Table III lists the disorders which were found among patients who returned one or more years after surgery. It is impossible to indicate the severity of these symptoms as many degrees of emotional tension and general physical disease influenced the patients. However, moderate to mild symptoms and disorders are included for emphasis. It is significant that among the patients who had vaginal plastic procedures, there did develop diseases of the colon, uterus, and ovaries. These diseases might well have contributed to the symptoms which led to surgery, and could have been discovered or prevented by the abdominal approach.

Urethral disorders are common after all gynecological surgery. Persistent trigonitis and urethritis are equally prevalent following all types of our

surgery, while stress incontinence has not been frequently encountered. Cervical disorders caused many late postoperative symptoms. Our experience suggests that the endocervix is one of the most sensitive areas of the female pelvis, and the trauma incident to conization, or partial amputation, often leads to disabling symptoms. This is further borne out by the relief of much lower abdominal pain after total hysterectomy.

Dyspareunia, vaginal stenosis, and mild degrees of recurrence of pelvic ligament relaxations were more frequent after vaginal hysterectomy and vaginal plastic cases. The vagina appeared to be better supported and more elastic in patients who had abdominal hysterectomy as compared with those who had vaginal plastic procedures. It is, of course, obvious that there would be more recurrence of vaginal symptoms following plastic procedures because the pelvic relaxations were much more severe in the latter group. We are positive, however, that our technique of hysterectomy with endopelvic support procedures gives an excellent vaginal support which produces no dyspareunia, and prevents subsequent pelvic relaxations which are known to follow hysterectomy all too frequently.

Accurate evaluation of emotional disorders is impossible but more painful fixations remained after the vaginal plastic operations than other gynecological surgery. One of our worst results was a painful retrodisplacement of the uterus with a definite syndrome of pelvic congestion[2] after an excellent-appearing Manchester operation. Psychiatric help is of little avail to the person who considers herself a surgical cripple. Added emphasis to the emotional side was brought out recently by a patient who had had a most successful vaginal hysterectomy with good support and no urinary symptoms, but who stated that there had been no sexual desire since the operation. It goes without saying that this would be a difficult problem to reverse in a woman of 52 years.

TABLE IV. COMPOSITE RESULTS OF SURGERY

TYPE OF SURGERY	TOTAL CASES	AVERAGE AGE	PATIENT'S CONDITION AFTER 1 OR MORE YEARS		
			ASYMPTOMATIC	SYMPTOMATIC	
				ORGANIC	FUNCTIONAL
Total hysterectomy	132	43	105	17	9
Subtotal hysterectomy	13	45	11	1	1
Vaginal hysterectomy	57	50	40	12	5
Hysterectomy and repair	34	41	28	3	3
Plastic repair only	100	38	59	34	14

Our series is, of course, small and statistically of little value, but bears out certain significant principles. Removal of the entire uterus with or without the adnexa eliminates a site of much pelvic pain, and relieves the functional bleeding with its accompanying anxiety (Table IV). This is further borne out by the painful disorders remaining after conization or partial amputation of the cervix. Removal of the uterus also allows the surgeon free access to the strong endopelvic fascia in construction of good pelvic support. On the

other hand, the vaginal plastic procedures must depend on the fascia below the bladder and over the rectum for most of the support. In vaginal hysterectomy, one has access to the stronger pelvic ligaments, but in the attempt to give good support, vaginal space is sacrificed in some cases. This becomes of increasing importance as the life span and vitality of our race are certainly increasing.

The average age of our patients (Table IV indicates that future childbearing is not a significant factor and certainly surgical skill has reduced the risk of hysterectomy to a very low figure.[3] We have encountered considerable shortening of the anterior vaginal wall in cases of anterior and posterior repair with resulting dyspareunia and urinary symptoms. This has led to the added technique of shortening the uterosacral ligaments in vaginal plastic work and thus further utilizing the supports of the uterus when there is a cystocele, rectocele, or perineal relaxation.

Recent publications[4-7] have applied many of these principles to vaginal hysterectomy as a superior method of pelvic repair, while others draw attention to the uterus as a site of much pelvic pain.[2] Care in selection of cases for pelvic surgery is repeatedly emphasized.[8-12] Gynecologists must deal with pathology of the reproductive organs, trauma from childbearing, plus the emotional stability of the patients. To accomplish these objectives, our surgery must remove pathology and do repair work which will be depended upon to keep our patients in a good physical and emotional state for a span of many years.

Summary and Conclusion

It is therefore increasingly evident from our studies that hysterectomy under proper indications leads to less persistent symptomatology than most other gynecological surgery. Its inclusion with pelvic plastic procedures at the proper age and with justifiable indications seems to improve the chances of lasting surgical cure from the pelvic relaxation. This is undoubtedly due to better exposure and repair of the endopelvic fascia incident to hysterectomy, and to the removal of a structure which can at any age be a site of many additional pathological and emotional symptoms.

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Discussion

DR. M. H. TALTY, Houston, Texas.—It is a pleasure to discuss this paper, which like its predecessor emphasizes some of the pitfalls of incomplete gynecological surgery. When one considers that the uterus, once a woman has passed the reproductive years of her life, or has borne her desired number of children, becomes a useless, and frequently a debilitating, and occasionally a dangerous, organ, the rationale of leaving behind all or part of that uterus, except under unusual circumstances, must be considered faulty surgical judgment. This is well exemplified in the essayists' presentation today and is a reminder that we can well heed.

Careful preoperative evaluation, as has been stressed today, of the complaints which bring the patient to us, of the pathology at hand, of what one hopes to accomplish, and then of the best method of reaching that goal with permanent benefits to the patient should be a routine procedure with everyone who undertakes to do pelvic surgery. Preoperative urological investigation should certainly never be neglected when there is the least hint that the cause of pelvic complaint might be within the urinary tract. There is still no substitute for sound surgical judgment in spite of the relative safety of pelvic surgery today.

Ideally, in the childbearing years, especially in the woman who has not yet attained her family, surgery should be delayed where it is possible and safe, with reassurance and conservative measures until such time as future childbearing is no longer an issue. Very occasionally, however, some surgical procedure is essential for relief of symptoms and/or pathology, and if that patient can be relieved, and her childbearing ability be preserved or improved, while she realizes the possibly temporizing nature of that surgery, I cannot help but feel it is justified, regardless of whether she must later return for a more extensive procedure. It goes without saying that there is a logical limit to such temporizing.

The choice of abdominal versus vaginal hysterectomy will always be an individual one. So long as the vaginal method is not shelved because of lack of familiarity with the procedure there cannot be too much controversy here.

It is my individual opinion that the vaginal approach, where feasible, offers better utilization of the pelvic ligaments, makes cystocele and rectocele repair simpler, and cuts down operative time and morbidity, especially where there is decensus plus symptomatic cystocele or cystourethrocele. The authors have well stressed the desirability of hysterectomy when pelvic surgery is undertaken, and the part it plays in cutting down the number of postoperative complaints and disorders. They must not be construed as advocating wholesale or unnecessary hysterectomy, but to leave the uterus behind, once its childbearing function ceases, is to invite these sequelae. The finding of three incidental endometrial carcinomas gives further emphasis to this conclusion. We still see too many carcinomas of the cervical stump and too many cervical carcinomas in women recently subjected to pelvic surgery. There can be no question as to their presence at the time of operation. Adequate work-up would bring proper and earlier treatment to the latter group and total hysterectomy will, we hope, soon make such an occurrence the rarity it should be.

UMBILICAL CORD CASUALTIES*

A Résumé With Presentation of Cases

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INTRAUTERINE life, sustained only by two small arteries and a tortuous vein coursing through a long flexible cord, hangs by a very delicate thread. That fetal fatalities occur so seldom from cord complications seems incredible. Gradually, however, it has become more apparent that cord abnormalities are frequently involved in Nature's plan for "survival of the fittest," especially in view of Javert and Barton's[12] findings in early and late abortions. They found 35 per cent of the available cords for study to be abnormal and inconsistent with life, with torsion occurring in 15.3 per cent, looping in 5.7 per cent, and knotting in 0.9 per cent. As pregnancy progresses the incidence of knotting apparently decreases, while the incidence of looping (and probably torsion) increases, if we are to refer to Lundgren and Boice's[13] figure of 0.3 per cent for knotting and Atwood's[1] figure of approximately 25 per cent for looping in the viable stages of pregnancy. These percentages probably reflect the fact that the more serious cord disorders kill the fetus in the early stages of pregnancy, leaving the lesser, though no less potentially dangerous, disorders until later gestation. It is these abnormalities which occur after viability has been reached with which we are concerned in this paper.

Intrauterine death from cord abnormalities most frequently involves anoxia of the fetus. Clementson[6] lists the general types of anoxia as anoxemic, histotoxic, cord obstruction, and anemic, the latter two being those in which cord complications may be directly involved. He further divides cord obstruction anoxia into the following causes: loops of cord about the fetus, prolapse of the cord, true knots, breech delivery with cord compression, and short cord. To this we might add torsion, new growths, and partial rupture of the cord with hematoma formation causing vascular obstruction. Anemic anoxia may be caused by complete laceration of the cord or its vessels with bleeding external to the cord's amniotic covering. Other sources of obstructive or anemic anoxia are so rare that their consideration is not warranted.

It is the purpose of this paper to summarize briefly, in so far as is possible, the incidence, associated fetal mortality, influencing factors, and general considerations of cord anoxia; to present two additional cases; and to discuss methods by which our fetal salvage rate may be increased.

Chief Causes of Cord Anoxia

New growths of the cord are commonly fibroids, dermoids, myxomas, myxosarcomas, hemangiomas, and related neoplasms. Urachal cysts are relatively

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even more common. Barry and associates[2] reviewed 130 cases of cord neoplasms and found a fetal mortality of 68.7 per cent, along with polyhydramnios and premature rupture of the membranes in 32 per cent. Dystocia was prone to occur and prolapse of the cord tumor has been noted. The true incidence of cord neoplasms is difficult to ascertain.

Short cord and its complications have been thoroughly reviewed by Rosen,[15] whose paper is heartily recommended to all obstetricians. Using 30 cm. or less to indicate *absolute* shortening, he found its incidence to be 0.78 per cent, while an additional 16.8 per cent showed *relative* shortening, in a total of 1,525 consecutive cases. Labor was not prolonged in the first or second stages, but fetal distress was increased by 25 per cent and the need for fetal resuscitation nearly doubled. A mortality rate of approximately 1 per cent of the fetus may be expected in this condition.

Breech delivery with cord compression is a rather common cause of fetal death, but since trauma is so often a concomitant feature in these cases, the exact incidence of fatal cord anoxia is unknown. Approximately 3 per cent of all deliveries are breech presentations and of these about 5 per cent result in fetal death.

Prolapse of the cord, followed by compression anoxia and fetal death, is a substantial factor. According to Bowen[3] the incidence of prolapse is 0.41 per cent with a fetal mortality of 53.52 per cent in these cases. Prolapse occurs frequently with breech presentation, transverse lie, hydrocephalus, and other disorders wherein the fetal "key" fails to fit the pelvic "lock" properly.

Torsion, looping, and true knotting of the fetal cord are, in my opinion, only varying degrees of the same general process, going from the simpler to the more complex, as it were. Twisting of the fetus on the cord as its axis will produce torsion. With appropriate circumstances this torsion may form a loop such as one obtains by twisting one end of a rope while the other end is fixed. Now suppose that the head or arm of the fetus is inadvertently caught in this loop. This process may be repeated and several loops of cord become fixed about the fetus. Or the fetus may find its way completely through a loop and then we have a true knot. By various combinations of torsion, looping, and subsequent knot formation we may find single overhand, double overhand, figure-eight, half-hitch, bowknots, and various other combinations.[9, 13] The fact that Javert and Barton[12] found torsion, looping, and knotting, respectively, in decreasing frequencies in early pregnancies would serve to substantiate the incidence to be expected with this hypothesis. Likewise, at term, the incidence of torsion is greatest, looping next most common, and knotting least common, as one would expect from the relative complexity of each process.

Torsion was regarded as the cause of death by the older pathologists, according to Edmonds.[7] The more modern view is that death antedates the torsion. Reasons for this difference of opinion are the lack of congestion and infarction in fetuses showing extreme torsion, and the observation that cords of macerated fetuses tend to be twisted more than the cords of nonmacerated ones. Yet, Herberz[10] reported the case of an infant with asphyxia resulting from torsion, that was delivered alive by cesarean section. While torsion probably rarely causes fetal death it is still a potential source of disaster with an unknown incidence.

Loops of the cord are more prone to cause anoxia than torsion, although as many as seven loops have been found about the neck of a surviving fetus. Clementson[6] found the cord oxygen and carbon dioxide blood levels were seriously altered by loops of the cord. Harrar and Buchanan[8] state that 14 of 38 unanticipated fetal deaths in the perineal stage were due to loops of cord about the fetal neck. While looping occurs in about 25 per cent of all de-

liveries,[17] there is usually no definite percentage of fetal mortality given, although it should not differ appreciably from the 1 per cent expected with a short cord.

True knots of the cord are most common in monoamniotic twins, where the incidence of true knots was 51.2 per cent and the associated fetal mortality 68 per cent, according to Boyle and Richter.[4] Lundgren and Boice[13] calculated an incidence of 0.3 per cent for knotting, with a fetal mortality of 53 per cent as an over-all figure. An ample length of cord plus sufficient Wharton's jelly and the pumping action of the fetal heart serve to maintain the patency of the cord vessels in almost all cases.

Rupture of the cord may be classified as partial or complete. Partial rupture involving a vessel will cause bleeding into Wharton's jelly and formation of a hematoma, resulting in obstructive anoxia if the amniotic covering of the cord remains intact. If this amniotic covering of the cord ruptures, then unrestrained bleeding from the cord vessels may cause rapid death of the fetus. Rupture of the cord in the last moments of delivery has a more fortuitous outlook than early rupture, for, although severe anemia of the infant may occur before the cord can be clamped, the mortality rate is lower. Rupture of the cord vessels may be secondary to velamentous insertion, a short cord, inflammation, trauma, or a sudden escape of excessive amniotic fluid. Its true incidence is indeterminate, but Williams[18] gives the incidence for velamentous insertion alone as 1 per cent of all types, and Novak[14] states that fetal death from rupture of the vessels in this condition is probably over 60 per cent.

Presentation of Cases

CASE 1.—Mrs. L. S., a 19-year-old para 0-0-0-0, was admitted to the hospital on Feb. 18, 1953, with painless vaginal bleeding of minimal degree. The expected date of confinement was May 23, 1953. Examination showed a 27 weeks' uterine gestation with normal fetal heart sounds. Pelvic examination was deferred because of a tentative diagnosis of placenta previa and two pints of blood were typed and cross-matched. The bleeding ceased on bed rest and heavy stilbestrol therapy. One week later the fetus lay in right sacroanterior position and still had normal heart sounds. Fetal movement ceased four days later, three days prior to resumption of bleeding and active labor on March 2, 1953. A 1 pound, 12 ounce, macerated, stillborn female infant was delivered spontaneously from a vertex position. The cord was discolored and showed three complete twists in the area immediately adjacent to the navel, where cord obstruction was obvious. No other cause for the intrauterine death was found. It was surmised that the fetal death had resulted from torsion, although further torsion may have occurred postmortem, in which case both schools of thought mentioned previously would be partially correct.

CASE 2.—Mrs. O. G., a 35-year-old para iii-0-ii-iii, who had not been seen prior to hospitalization, was admitted on June 28, 1951, in labor and at term. Labor had begun some four hours prior to admission and she had felt fetal movement at least until early in the labor. On admission she was taken directly to the delivery room where she delivered a nonmacerated, stillborn, term-sized male infant exactly 12 minutes later. The cord had a single true knot, fairly snugly tied, with complete obstruction of the vascular elements and located midway between the fetus and the placenta. With the knot intact, the cord measured 15 cm. and with it untied, 20 cm. There had been insufficient time prior to delivery for auscultation of the fetal heart. There seemed to be little doubt but that the short cord and the true knot combined to cause the death of this infant.

Comment

The first decision necessary is whether an increased fetal salvage can be expected in these cases by a planned course of action. On the basis of the previous figures given for the various cord complications, and ignoring those

for which figures were not available, we might expect fetal death to occur in 1.23 per cent of all deliveries. This is slightly higher than the 0.7 per cent incidence Cannell and Horne[5] found for "anoxic" deaths in 4,294 births. Taking an average figure of 1 per cent as the incidence of fetal deaths from cord anoxia would seem a safe assumption. Although many of these deaths are nonpreventable, with routine planned pregnancy care it is felt that one-half of this 1.0 per cent might be salvaged. In my opinion obstetrics has advanced to the stage where even this small figure is of significance.

Having reached this decision, the problem of early diagnosis arises. The diagnosis of intrauterine anoxia from cord complications resolves about suspecting it in certain conditions, frequent and careful auscultation of the fetal heart, and adequate abdominal, vaginal, and x-ray examinations, including special techniques to be discussed later. During late gestation and prior to labor there are several indications of possible cord complications necessitating close observation of the patient. Excessive movement of a fetus, followed by cessation of all movement, may often mean fetal death.[9] Any fetus, however, that frequently changes position, as indicated by routine office examinations, is a candidate for torsion, looping, or knotting of the cord. If the presenting part is high at term one should suspect a short cord or some form of placenta previa, which is often associated with a velamentous insertion of the cord. Malposition and breech presentation predispose to cord prolapse. Rosen[15] mentions Hamilton's test, in which pushing a high head into the pelvis may change a normal heartbeat to one of less than 80 beats per minute. If, on then releasing the pressure, the heart rate rises to over 120 beats per minute there is presumptive evidence of a short cord. Israel,[11] discussing Rosen's article, states that a short cord from loops about the fetal neck may at times be diagnosed by x-ray evidence of angulation of the fetal head, associated with a high placenta, and after excluding all other causes for failure of descent. X-ray localization of the placenta, pelvimetry, and studies for position and congenital anomaly of the fetus are advisable routinely. Last, sterile vaginal examination a week or two prior to the expected date of confinement may be very revealing, and will give one a basic knowledge of the pelvic status should subsequent cord pathology occur.

During labor much information can be gained in appropriate cases by repetition of many of these tests. Sterile vaginal examination should be done at the onset of labor, after spontaneous rupture of the membranes, and, if there is evidence of fetal distress, in search of cord presentation or prolapse, vasa previa, and for information regarding fetal position and the progress of labor. Bloody amniotic fluid, especially if associated with rupture of the membranes, should lead to examination of the amniotic fluid for fetal nucleated red blood cells[16] and to careful auscultation of the fetal heart, as evidence of a ruptured cord or vessel. Meconium-stained amniotic fluid, particularly with vertex positions, may indicate fetal distress. Auscultation of the fetal heart every 15 to 30 minutes is essential and if significant changes are noted the tests to be described later, using oxygen, deep Trendelenburg position of the mother, and digital elevation of the presenting part, are indicated.

The final diagnosis of fetal anoxia from any cord complication usually hinges on the auscultation of the fetal heart for rate, rhythm, and intensity, although the latter is often unreliable because it is so readily altered by a change in the position of the fetus. In my experience the following progressive sequence of changes has been the commonest indication of fetal distress as related to cord disorders. As a rule, the first finding is a progressive increase in the fetal heart rate, during uterine contractions as labor advances, to over 160 beats per minute and lasting longer and longer after the contraction subsides. Usually the rate is regular but with higher rates it may become irregular. On occasion, if the uterine contractions are severe and prolonged, this initial tachycardia may be followed by excessive slowing to rates below 110 or 120 beats per minute even before cessation of the contraction. With further and more severe anoxia one may expect the fetal heart rate to drop below 100 beats per minute, with less and less initial tachycardia during contractions and with more frequent cardiac irregularities. At this stage the infant's condition is indeed critical and the administration of oxygen to the mother is essential, both as therapy and to afford relief to the fetus. If oxygen therapy serves partially or completely to correct the cardiac disorder the fetus is still capable of responding and is presumably not seriously damaged. If no such response occurs then serious damage is indicated, or is imminent, and unless delivery is accomplished within the next few minutes permanent injury or death of the fetus may result. Auscultation of the fetal heart with the patient in deep Trendelenburg position and with the presenting part displaced upward digitally may also give valuable prognoses in certain cord disorders, such as prolapse or compression of the cord, and in pathological shortening of the cord. Administration of oxygen, Trendelenburg or knee-chest position, and digital elevation of the presenting part may also maintain fetal life until definitive therapy can be accomplished.

Treatment

When fetal cord anoxia is diagnosed the cause should be found, if possible, for often the treatment hinges on this factor of etiology. In general, the treatment consists of the most expedient means of delivery, maintaining due caution regarding both fetal and maternal trauma, but with *time* of prime importance. A persistent fetal heart rate of over 180 or under 90 beats per minute, especially if associated with cardiac irregularity or excessive fetal motion, is an indication for prompt action. Lesser degrees of anoxia allow for careful temporization. General or spinal anesthesia may be necessary to prevent expulsive efforts of the mother from increasing the cord anoxia. Preparations for both vaginal and abdominal delivery should be made in all cases and the decision as to which method should be used must give due consideration to the following: the degree of anoxia evident in the fetus; the fetal position and station of the presenting part; congenital anomalies of the fetus; the type of cord disorder involved; the age, parity, and obstetrical record of the mother; the rapidity of the labor to the present time and the estimated time remaining

until delivery; the status of the membranes and cervix; the adequacy of the pelvis; and coincidental complications of the pregnancy and labor. A pediatrician should be present at the delivery when possible.

Vaginal delivery should continue to be the treatment of choice in the majority of cases, notably when nonprogressive, mild to moderate fetal anoxia is present and delivery is anticipated within the next thirty to sixty minutes; or at times when fetal distress is severe, but delivery is expected within a matter of minutes; or with dead or congenitally malformed fetuses. Usually nothing more than close observation and the previously mentioned general measures will be required, but additional steps may be necessary. Often, artificial rupture of the membranes will hasten the latter part of labor, but it is contraindicated in vasa previa with a live fetus unless delivery is anticipated immediately. The use of Willett forceps may occasionally be of value after replacement of a prolapsed cord or with a dead fetus, but scalp traction may increase cord anoxia in the other disorders and should therefore be used cautiously and only after an etiological diagnosis has been made. "Bagging" a patient carries too high a fetal mortality to be recommended. Manual replacement of a prolapsed cord may be attempted but recurrence should be anticipated, and if it occurs then more definitive therapy is indicated. With a breech presentation at the "perineal" stage simple breech extraction is advisable, but internal podalic version followed by breech extraction involves excessive hazards to both fetus and mother. Prolapsed cord with a well-dilated cervix in a multipara with a transverse lie of the fetus may best be handled by version and extraction in some cases. Low forceps may be used to expedite matters in vertex positions. Dührssen's incisions may also be advantageous in cases in which the head is low in the pelvis, with at least 6 cm. of cervical dilatation and with complete cervical effacement, but they are often contraindicated in breech presentations because of the usually poor cervical effacement in these cases. One must not forget that in the face of moderate to severe fetal distress, even with the presenting part low and the cervix well dilated, the further descent essential for vaginal delivery may increase the fetal anoxia to a nonreversible stage. Unless delivery can be terminated immediately, vaginal delivery may be ill advised in these cases.

I feel that a sane liberalization of fetal indications for cesarean section, done by competent obstetricians and after adequate consultation (when time permits), will be necessary for highest fetal salvage. In good hands the increased maternal risk should be minimal. We must remember that the indication is for *fetal* distress, however, and not for *obstetrician* distress. In general, cesarean section will be advisable in cases of progressive, moderate to severe cord anoxia when delivery is not anticipated within fifteen to thirty minutes; when fetal distress will be seriously increased by further descent of the presenting part; when moderate fetal distress is associated with other complications such as previous sterility of the mother, an elderly primipara, and faulty position of the fetus, or an anticipated long labor; when prolapse of the cord occurs or recurs and delivery is not imminent; and when vasa previa is

diagnosed with a live fetus prior to rupture of the vessels or inevitable fetal death. Many "perineal" fetal deaths are cases of "neglected" cord obstruction in fetuses that should have been delivered abdominally earlier.

Although generalities regarding indications for both vaginal and abdominal delivery in cases of cord anoxia may be made, it must be thoroughly emphasized that individualization of each case is essential if the best results are to be obtained. The obstetrician must likewise fit the handling of each case to his own particular capabilities and experience.

Summary and Conclusions

1. The more common causes of fetal cord anoxia have been reviewed and the estimated incidence of fetal fatality in these cases has been placed at 1 per cent of all deliveries.

2. It has been estimated that the fetal salvage may be increased by one live birth per 200 deliveries if cord anoxia is searched for diligently. This requires close observation during late gestation and during labor, the utilization of x-ray studies routinely, if possible, the use of other described tests, and the judicious evaluation of the entire situation when cord anoxia is found.

3. The treatment of fetal anoxia from cord disorders is briefly discussed and a slight liberalization of indications for cesarean section, done by competent obstetricians, is suggested. The advantages to be gained far outweigh the maternal complications expected in good hands. The use of intrauterine bags is discouraged and internal podalic version with subsequent breech extraction should be relegated to less frequent usage because of its inherent dangers. Otherwise, treatment is in general agreement with standard principles of obstetrical practice.

4. The fact that treatment must be individualized in each case has been stressed.

5. Two typical cases of cord pathology capable of causing fetal death from anoxia have been presented.

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Discussion

DR. J. E. KANATSER, Wichita Falls, Texas.—The essayist has covered his topic so thoroughly from the etiological and pathological standpoints that I have nothing further to add along these lines; however, I want to open the discussion of his paper by outlining my viewpoints as to the management of these obstetrical complications—especially prolapsed cord —and then making a few general remarks on the contents of his paper.

All of us have had patients with prolapsed cords, after the cervix was completely dilated or near completely dilated, and have obtained living babies. In these instances the membranes remained intact, and the labors were usually short, and the baby was quickly delivered either spontaneously or by properly applied forceps.

I am sure that each of us has lost term, or near-term babies because the fetal cord was wrapped one or more times around the baby's neck—this is more likely to be the direct cause of fetal death, when it occurs with breech presentation. And the tragic part of it is that we have no definite means of making a positive diagnosis in such complications, except by close observation of the fetal heart tones—and this unfortunately is not always dependable, especially in the delivery of the aftercoming head in breech cases.

Proper management of patients with prolapsed cords depends upon many factors, such as the degree of cervical dilatation, the duration of gestation, the general condition of the mother and baby, the parity of the patient, and also whether or not any degree of disproportion coexists and whether or not the patient is in active labor. The most important of all of these factors, in my opinion, however, is the amount of dilatation of the cervix, the duration of the gestation, and the condition of the mother and baby.

I firmly believe that patients with viable babies and prolapsed cords should be handled by quick section, unless the cervix is completely or nearly completely dilated, provided the fetal heart tones are still good—and this type of therapy is especially valuable if that patient is a primipara and has a cephalic presentation. The Trendelenburg position and free use of oxygen are invaluable for such patients.

In case we delay delivery of the baby until the fetal heart tones are extremely slow or extra fast, even quick section may be too late because in these instances severe brain damage may have already occurred, and we would be delivering a baby that may be none too alert mentally, which really would be worse than a stillbirth.

As a prophylactic measure against prolapsed cords, we should not be too eager to induce labor by artificially rupturing the membranes unless ideal conditions are present, such as cephalic presentation, the absence of any degree of disproportion, good engagement within the maternal pelvis, an extremely ripe cervix, and also the certainty that we are not handling a patient with a so-called forelying cord.

I have had several viable babies with natural knots, but fortunately none of these knots were tied tightly enough to result in fetal death. Like every obstetrician present at this meeting, however, I have had several cases of nonviable babies, where pregnancy terminated spontaneously with macerated fetuses, and close examination led us to believe that intrauterine death was due to cord abnormalities.

It has been my impression that prolapse of the cord, or natural knots in the cord were more likely to be the result of the cord being too long rather than too short.

Dührssen's incisions of the cervix can easily lead to lacerative extensions into the lower uterine segment, with uncontrollable uterine bleeding. Therefore, I prefer section, if the baby is viable and the cord has prolapsed, provided the fetal heart tones are good, instead of Dührssen's incisions, unless the cervix is well effaced and fairly well dilated.

Torsion of the fetal cord has been a very rare complication in my obstetrical practice —or perhaps I have had such cases and failed to recognize them.

TRAUMATIC LACERATION OF UTERINE SUPPORT

The Clinical Syndrome and the Operative Treatment

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THE postpartum pelvic cripple is frequently suffering from a clinical entity to be described as the "universal-joint" cervix. This particular form of distress is not alone confined to the cervix and its anatomical supports, but occurs in the basic uterine support as well. Therapy is now well established and results obtained to date have been gratifying.

In 1949 Taylor[1-3] presented a series of three papers under the encompassing title of "Vascular Congestion and Hyperemia." The author was concerned with the breast and the complete female generative tract. This work has become a well-established milestone on the subject of pelvic pain. Cases were completely and objectively analyzed, and the previous literature on this popular subject was exhaustively reviewed.

The present paper is not intended in any way to supplement such a monumental work. Rather, the clinical syndrome to be described is offered as a plausible explanation for a clinical observation mentioned, but not completely explained, by either Taylor or by his predecessor, Condamin.[4]

The "universal-joint" cervix is developed as the result of lacerations of the fascial tissue layers in the broad and Mackenrodt's ligaments. The lacerations usually result from a surgically traumatic or precipitate delivery, and are occasionally noted subsequent to criminal abortion technique (primarily excessive vaginal packing).

The patient is first seen with the standard complaints which develop from pelvic congestion: primarily, dyspareunia, dysmenorrhea, and a feeling of being excessively tired. The complaints are usually of a secondary or acquired nature. For instance, patients can frequently date their acquired dyspareunia to one particular delivery in the case of a family with three or four children. The basic coital distress arises from deep penetration of the penis. These patients describe the pain associated with intercourse as if their husbands hit something with deep penile penetration.

The acquired dysmenorrhea is also usually pinpointed by one particular obstetrical event. Thereafter, periods are gradually lengthened in amount of flow and frequently the passage of clotted blood is first noted. Cramping becomes progressively more of a clinical distress, and usually has its onset at about the time menstrual flow is first noted. There is in addition a "com-

pletely exhausted'' feeling, emphasized during the first two or three days of menstrual flow, but of major concern at all times to a mother with young children.

There are also the irritations of a relatively constant, nagging backache, a throbbing, generalized pelvic aching, and a sense that ''everything is falling out.'' These primary distress features are emphasized by the demands of a long day of housework, or any employment that necessitates a good deal of time on one's feet.

The basic pathology is confined to the pelvis. The striking features of the bimanual examination are the position of the corpus (always in severe third-degree retroversion), and the particular feeling resulting from manipulation of the cervix. The cervix feels just as if it were being rotated as a ''universal joint.'' The juncture of the cervix to the lower uterine segment of the corpus is ill defined. The cervix may be moved in any direction, up, down, laterally and in an anteroposterior plane with minimal, if any, responsive movement in the corpus. The feeling is one of an exaggerated Hegar's[5] sign of early pregnancy, in which the cervix seems to move independently of the attached corpus.

In addition to the ''universal-joint'' feeling of the cervix, there is frequently severe pain associated with particular cervical movement. This pain is primarily associated with pushing the cervix in an upward plane. In the more severe cases (either advanced bilateral broad ligament lacerations or presenting complaints of five years' duration), even mild lateral motion of the cervix will occasion a severe pain response.

The corpus will appear to be from about once to twice increased over normal size. Pressure against the corpus to reduce the third-degree retroversion (which is usually readily accomplished) will also produce a severe pain response. Upward pressure on the cervix or pressure in the cul-de-sac against the corpus will be described by the patient as ''just like the pain I have with intercourse.''

The ovaries may frequently be palpated as prolapsed into the cul-de-sac. When present, true ovarian pain is severely elicited with pressure on the adnexa. In all probability this ovarian prolapse is purely a secondary result of the severe retroversion of the corpus, and consequent constant tension on the infundibulopelvic ligaments. Frequently, subsequent to the onset of the resultant congestion and tissue hyperemia, symptoms of definite ovarian failure have been noted.

Presenting Complaints

Exploratory operations have been performed on 28 patients with a preoperative diagnosis of ''universal-joint'' disease. The diagnoses were individually achieved by a combination of positive history and pelvic findings. A detailed study of the complaints associated with the present illness of the 28 patients under consideration is presented in Table I. The presenting complaints will be discussed in order of their frequency when the significant details of the material are described.

TABLE I. PRESENTING COMPLAINTS (28 CASES)

SYMPTOMS DESCRIBED	NO. CASES
1. Dyspareunia	24
2. Excessive physical fatigue	24
3. Dysmenorrhea	22
4. Generalized pelvic distress	21
5. Specific localization of pelvic distress	19
6. Emotional instability	16
7. Metrorrhagia	12
8. Chronic headaches (occipital)	9
9. Menorrhagia	5
10. Genitourinary symptoms	5
11. Chronic nonspecific vaginal discharge	5
12. Premenstrual defecation pain	4

Dyspareunia.—Twenty-four of the patients presented this complaint. One patient stated that she had always had dyspareunia but that the degree of discomfort had become much worse after a particular obstetrical accident. The remaining patients had almost identical histories. The pain is always elicited with deep penetration of the penis. Several of the women involved stated that only as the male partner approached his climax, and the thrust was correspondingly deeper and stronger, was the severe pain elicited. Universally, the distress was described "as though he hit something with the penis." The distress is described as a severe stabbing pain in the midline, deep in the pelvis. Frequently minor pelvic distress lasts for hours after intercourse. Patients will occasionally notice a minimal aching or "hurting low down" the morning following coitus.

Excessive Fatigue.—Equally as frequently encountered as a primary complaint was the syndrome of excessive fatigue (24 of 28). The patients were more concerned with this particular distress than any other recorded in Table I. Many individuals complained bitterly that the most crippling part of the entire process was the fact that they could not meet their responsibilities because they "tired so easily." The excessive fatigue of the first six weeks post partum, or of the untreated menopausal syndrome, is reduplicated here. The patients felt that their families suffered, and that their children were not as well cared for as could be expected, simply because the least expended effort tired the women involved to a point of near exhaustion.

Dysmenorrhea.—Moderate to severe dysmenorrhea was recorded for 22 of the 28 patients in the series. Six of these patients described significant menstrual distress prior to their obstetrical experiences. Thus a total of 16 of the 28 patients developed moderate to severe dysmenorrhea associated with the "universal-joint" syndrome. The distress of lower abdominal aching and the onset of cramping usually is noted from 48 to 72 hours before onset of flow and continues until the flow is well established, frequently to the second day of the period. Nausea and headaches (primarily occipital) were also reported associated with the menstrual period.

Pelvic Ache—Specific or Generalized.—Symptoms of generalized pelvic aching frequently reported associated with uterine retroversion and pelvic congestion were present as a presenting complaint in 21 of the 28 patients. Included in this group were 19 patients who also complained of a specific form of pelvic distress in addition to the generalized complaints of pelvic loginess, fullness, or a "feeling that everything might fall out." Of the 19 women with a specific form of distress, 7 complained particularly of direct suprapubic aching and described mild but chronic midline tenderness. The remaining 12 individuals complained of low backache or of coccygodynia-like symptoms, always made worse by physical exertion or any situation requiring long periods of standing.

Emotional Instability.—By far the most difficult of the presenting symptoms to evaluate were those suggesting emotional instability. Sixteen of the patients in the series made mention of symptoms that could be grouped under this general classification. Complaints varied from crying easily to severe depressions and even to vocalized interest in suicide. The only consistency noted in this complaint group was the very interesting fact that the longer the history of distress, the more frequent were the symptoms of emotional instability. No individual in the entire series whose original obstetrical distress dated back for a period of five years or more escaped being recorded positively in this emotional instability group.

Menorrhagia and Metrorrhagia.—These complaints of frequent or excessive menstrual flow were recorded in 5 and 12 patients of the series, respectively. Menorrhagia was not described without an accompanying metrorrhagia complaint. However, metrorrhagia was present 7 times as a single bleeding-type complaint. An increase beyond the established pattern in either duration or amount of menstrual flow is frequently seen in this "universal-joint" syndrome.

The remainder of the presenting complaints were not deemed of major moment or particularly significant in association with the "universal-joint" syndrome. Despite a significant percentage of surgical obstetrical distress associated with the onset of "universal-joint" symptoms, only 5 patients subsequently presented positive histories of genitourinary complaints.

Obstetrical History

One of the vital concerns in establishing a diagnosis of the "universal-joint" syndrome is a detailed obstetrical history. The positive findings in the obstetrical history review of the 28 reported cases are listed in Table II. This history table records the salient fact that, in 22 of the 28 cases, the onset of pelvic distress directly followed one particular obstetrical event. This untoward event may be classified as either a surgical obstetrical situation, an obstetrical accident, or even poor obstetrical technique.

TABLE II. OBSTETRICAL HISTORY (28 CASES)

1. No positive history of obstetrical distress	9
2. Precipitate delivery	7
3. Difficult forceps delivery	6
4. Complicated breech delivery	3
5. Postmature infant (10 pounds)	1
6. Severe postpartum hemorrhage with uterine and vaginal packing	1
7. Criminal abortion (vaginal packing technique)	1

1. No Positive History of Obstetrical Distress.—There was no positive history of previous obstetrical distress obtained from 9 patients. It is important to point out, however, that some patients would not be in a position to report untoward obstetrical results. An example of this practice of "keeping the true story from Mother" is the fact that 3 of the 9 patients who were unaware of any unusual obstetrical event in their past history were able to date specifically the onset of their pelvic distress to one particular delivery. There were also suggestive, although admittedly not positive, histories of obstetrical distress obtained in a backhanded manner from 4 of these 9 patients. Three patients described obstetrical tragedies with fetal death during delivery or in the first twelve hours post partum, and one patient told of a broken clavicle in a newborn infant subsequent to delivery.

2. Precipitate Delivery.—Seven of the patients described precipitate deliveries. Three deliveries were unattended until delivery of the baby's head

was accomplished. Specific interference with the normal process of delivery was recorded in the remaining 4 patients. Three of these patients described in specific detail nurses or house-staff physicians holding their legs together until the attending physician could arrive. One patient described the nurse holding the baby's head back manually until the physician in question put in his appearance. All of the patients described in the category of precipitation specifically date the onset of the major portion of their "universal-joint" symptoms to this particular obstetrical event.

3. Difficult Forceps Delivery.—Six patients could directly pinpoint the onset of their symptoms to a difficult forceps delivery. Such comments as "the baby's head was turned the wrong way" or "the doctor said I shouldn't ever have any more babies because my pelvis is so small" are indicative of the problems encountered by the physician in charge of the case. Also of interest is the suggestive history of obstetrical distress contained in the facts that one of these six difficult forceps deliveries resulted in a spastic child, and in one other instance a skull fracture was reported.

4. Complicated Breech Delivery.—Three patients in the series could date the onset of their pelvic distress to breech deliveries. There were no other significant details elicited from these patients concerning the deliveries, other than the baby's weight. Two of the babies were over 8 pounds in birth weight.

5. Postmature Infant.—The delivery of a postmature infant weighing 10 pounds pinpointed the pelvic distress of one individual in the series, although no history of trauma could be elicited.

6 and 7. Extensive Vaginal Packing.—Two patients dated their pelvic distress to similar obstetrical circumstances. Both noted the onset of their symptoms subsequent to episodes of extensive vaginal packing. The first patient described a severe postpartum hemorrhage with two attempts at uterine and vaginal packing before the bleeding could be brought under control. The second patient, a young girl with a history of a criminal abortion, described an extensive vaginal packing technique as the method used to stimulate labor, and subsequently to cause abortion. All symptoms of pelvic distress are directly related to these packing episodes.

Pelvic Pathology

At the operating table, the pelvic findings associated with the "universal-joint" cervix are relatively constant as shown in Table III. The presence of free fluid in the pelvis at laparotomy is worthy of particular note and comment.

TABLE III. PELVIC PATHOLOGY (28 CASES)

PATHOLOGY DEMONSTRATED	TOTAL CASES POSITIVE REPORT	
1. Third-degree retroversion of the uterus	28	
2. Serous fluid in pelvis (30-80 c.c.)	27	
3. Bilateral broad ligament laceration	22	
4. Unilateral broad ligament laceration	6	
Right		4
Left		2
5. Unilateral sacrouterine ligament laceration	5	
Right		3
Left		2
6. Bilateral sacrouterine ligament laceration	1	

1. Third-Degree Retroversion of Uterus.—The corpus in these "universal-joint" cases is always in third-degree retroversion. Usually the uterus is at least once increased over normal size. The walls of the corpus are soft and

the entire organ has the purplish-red cast so frequently noted in hemostasis. When the corpus is brought forward to allow repair work on the broad ligament lacerations, it shrinks in size, and will usually have lost at least a third of the original size before the abdominal component of the surgery can be completed. The prolapse of the ovaries into the cul-de-sac is also worthy of comment. Here too, a notable increase in size over the expected norm is frequently encountered. The ovaries otherwise show no characteristic change other than a definitely increased incidence of small follicular cyst formation. This may well be evidence of minimal failure due to mechanical interference with effective blood supply.

2. Serous Fluid in Pelvis.—With one exception, free fluid was demonstrated in the pelvis. This fluid is mentioned by both Taylor and Condamin in their discussions of pelvic congestion. In three cases the fluid was blood-tinged, but usually the fluid is straw colored and present in amounts varying from 30 to 75 or 80 c.c. The bowel and entire pelvic peritoneum are injected and marked venous patterns are always demonstrable. During the surgical repair in one case of severe bilateral broad ligament lacerations, a steady weeping from the wound in the posterior peritoneum could be constantly demonstrated. A discussion of the etiology of this fluid in the pelvis will be carried out later in the article.

3 and 4. Broad Ligament Laceration.—Bilateral broad ligament lacerations were demonstrated in 22 of the 28 cases operated upon. Four of the remaining 6 patients had unilateral lacerations confined to the right broad ligament, while the final 2 cases showed left broad ligament lacerations.

5 and 6. Sacrouterine Ligament Laceration.—An extension of the lacerations to include the sacrouterine ligaments was described in a total of 6 cases. In 3 cases it was in the right sacrouterine ligament, in 2 in the left, and in one instance bilateral tears were noted.

Surgical Procedures

The individual surgical procedures carried out on these patients are listed in Table IV. With the exception of an explanation of the uterine suspension and cervical conization procedures employed, the table is self-explanatory.

TABLE IV. SURGICAL PROCEDURES ACCOMPLISHED (28 CASES)

PROCEDURES	NO. OF CASES POSITIVE REPORT
1. Repair of broad ligament lacerations	28
2. Gilliam-Crossen suspension	23
3. Routine appendectomy	21
4. Dilatation and curettage	12
5. Conization of the cervix	8
6. Repair of sacrouterine ligament lacerations	6
7. Perineorrhaphy	3
8. Cystocele repair (from above)	2
9. Bilateral tubal ligations	2
10. Cystocele repair (from below)	1
11. Removal of endometrial implants from cul-de-sac and ovaries	1

1 and 6. Repair of Broad Ligament and Sacrouterine Ligament Lacerations.—The repair technique for the broad ligament and sacrouterine ligament lacerations will be described in the section dealing with surgical technique.

2. Gilliam-Crossen Suspension.—The first 23 patients in whom the broad and sacrouterine ligaments were repaired also routinely had suspensions,

using the Gilliam-Crossen technique. This additional technique of uterine support was used primarily because we were not sufficiently sure of our ground to rely on the ligament repair alone. The last 5 cases, however, had no suspension technique added to the repairs of the lacerations, and their results to date have been excellent. At present writing, suspension technique is not planned as a supplement to broad ligament repair in future cases unless support occasioned from this repair is obviously inadequate in any particular case.

4. Dilatation and Curettage.—A routine curettage was carried out on all patients whose presenting complaints contained positive statements in respect to menorrhagia and/or metrorrhagia (12 cases). Four instances of benign endometrial hyperplasia were noted, and one case merited a diagnosis of endometrial polyps (glandular). Otherwise the curettings were not remarkable.

5. Conization of the Cervix.—In 8 cases lacerations of the cervix or widespread endocervicitis were such that conization techniques were deemed indicated. These procedures were carried out prior to laparotomy in order to provide easy access to the cervix. T-tube drains were employed and removed on the eighth postoperative day. Results were universally satisfactory from an anatomical point of view. One clinical failure was noted in this group and will be discussed later.

7 and 8. Perineorrhaphy and Repair of Cystocele.—Despite the widespread pelvic tissue laceration demonstrated in the 28 cases under consideration, only 3 cases were deemed candidates for anterior and posterior colporrhaphy techniques. Two of the anterior repairs were easily accomplished from above following techniques previously reported[6] while the third anterior repair was done from below due to widespread pelvic varicosities. The posterior repairs were carried out from below following established techniques without incident.

Pathological Anatomy and Surgical Correction Techniques

The basic anatomical lesion involved in the "universal-joint" cervix is a laceration of the broad ligament. These lacerations may occasionally be unilateral (6 of 28 cases), but are usually bilateral (22 of 28 cases). The lacerations may and frequently do extend through the base of the broad ligament (Mackenrodt's ligament) as drawn in Fig. 1. Further extension to include the sacrouterine ligaments was occasionally noted (6 of 28 cases) (Fig. 2). This sacrouterine extension was bilaterally present in only one instance.

If the basic pathology is viewed from the posterior surface of the broad ligament (Figs. 1 and 2) the rent in the posterior peritoneum is easily demonstrated. This tear in the peritoneal surface may be as widespread as the basic fascial lesion, or may be present only as pinpointlike abrasions through which the usual serous weeping of the wound occurs. The larger the peritoneal tear, the greater the amount of serous fluid found in the cul-de-sac, and the greater the degree of serosal surface peritoneal irritation demonstrable on bowel wall or parietal peritoneal surfaces.

The fascial tears demonstrated in Figs. 1 and 2 are, of course, the basic cause for the constant finding of the markedly retroverted (always third-degree) uterus. These tears in the fascia are usually clean-cut in character, and there is a marked retraction of the torn fascial edges in the direction of their attachments.

As opposed to the picture diagrammed for illustration purposes in Figs. 1 and 2, the fascial layer on the uterine side of the tear retracts back toward the corpus, and frequently may be demonstrated only in close apposition to the lateral wall of the corpus. The lateral fascial layer retracts to an even greater degree. It is frequently necessary to approach the wall of the bony

Fig. 1. Fig. 2.

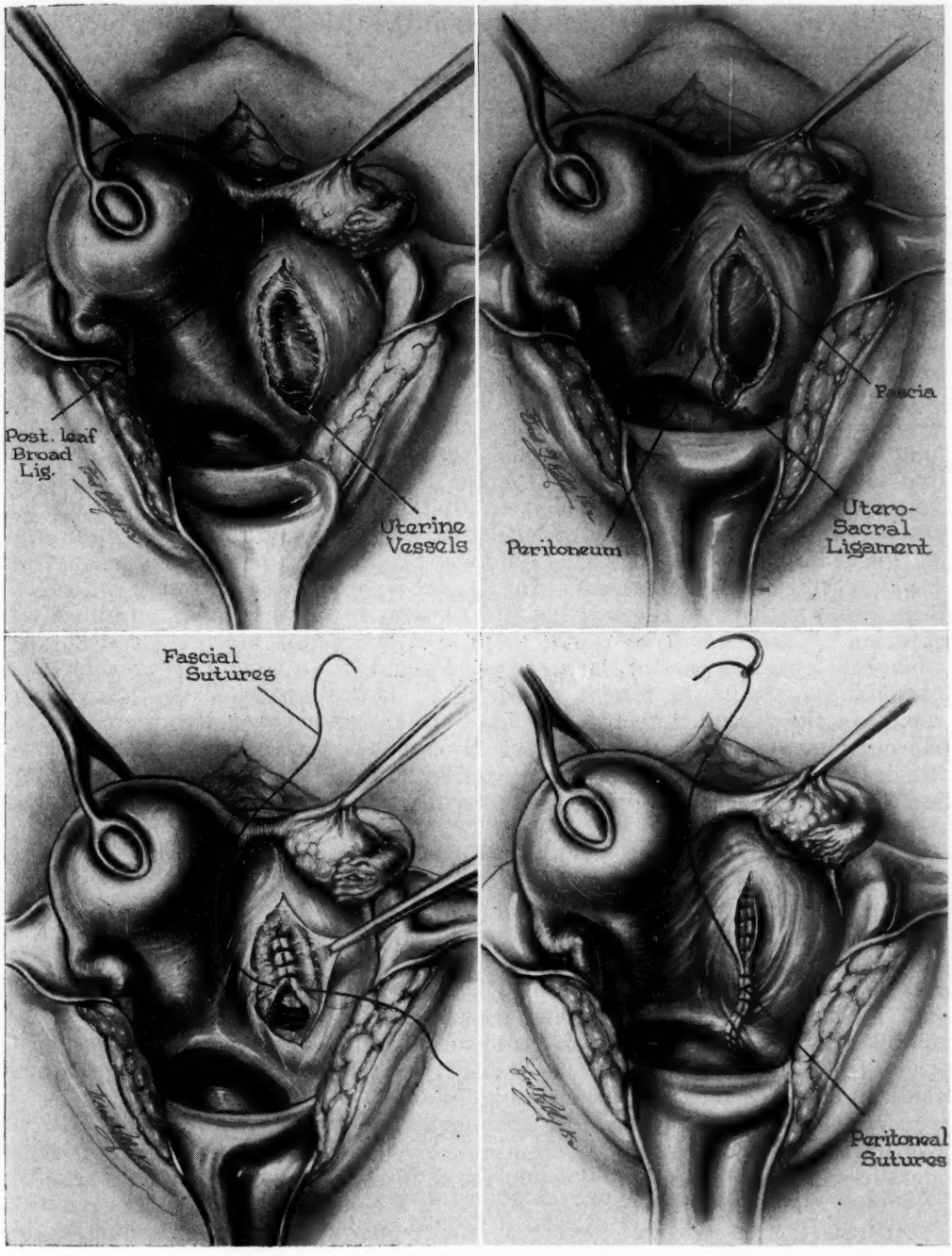

Fig. 3. Fig. 4.

Fig. 1.—View of laceration in posterior leaf of right broad ligament showing involvement of both peritoneal and fascial layers. Note beginning prolapse of uterine vessels.

Fig. 2.—Same as Fig. 1. Note that laceration has been extended in this view to include right sacrouterine ligament with more advanced prolapse of major vessels.

Fig. 3.—View of posterior leaf of right broad ligament after peritoneal laceration has been extended by surgical dissection. The laceration in the fascial planes is being repaired with interrupted No. 00 chromic catgut.

Fig. 4.—Same as Fig. 3. Terminal closing of wound in peritoneum. Laceration closed from base below the sacrouterine ligament.

pelvis before the retracted fascial layer can be uncovered. Despite the wide degree of separation frequently demonstrated, the torn edges of the fascia are easily approximated without tension at the time of surgical correction of the defect.

The position of the major uterine vessels is of moment in this condition and should be considered in some detail. If the tear in the posterior leaf of the broad ligament is complete (both fascial and peritoneal layers widely lacerated), the uterine vessels will prolapse through the rent (Figs. 1 and 2). In this situation the vessels will be discovered pulsating freely, completely uncovered and unprotected in the cul-de-sac, when the uterus is elevated from its third-degree retroverted position. These patients are the ones who have the most advanced clinical symptoms and are, in every sense, pelvic cripples. The vessels are not involved in the actual traumatic laceration, although the fascial plane through which they run may be completely destroyed.

The surgical correction technique, illustrated in Figs. 3 and 4, necessary to remedy the broad ligament pathology is simplicity itself.

The rent in the peritoneal layer is widely dissected as illustrated in Fig. 3. This provides easier access to the usually widely separated fascial remnants. Once the field is prepared, the fascial elements are brought to the midline and sutured into position with No. 00 chromic catgut. Care must be taken in suturing the fascial element that has retracted toward the lateral uterine wall. It is very easy to enter the lateral vessel plexus of the uterus at this point. The slightest mistake in either dissection or suturing may occasion a widespread hematoma. The fascial layer retracted toward the pelvic brim easily returns to the midline and remains in place without tension after suturing. Care should be taken to protect the major uterine blood supply when repairing the base of the incision. Fascial repair should ensure adequate vessel support without torsion or kinking. It is perhaps easier to start the repair in the fascial defect at the base of the lesion, even if it includes the sacrouterine ligament, than to work from above toward the pelvic floor as illustrated in Fig. 3. Frequently an initial suture placed in the center of the lesion is useful for retraction, and provides easier access to the base of the defect.

The rent in the peritoneum, either originally present or sufficiently enlarged to provide exposure as a first step in the surgery, is then repaired with a simple running suture of No. 00 chromic catgut. An excess of peritoneum is always available. Tension on the repair site has never been noted.

Careful inspection of the opposite broad ligament should always be carried out, even though the peritoneal layer may be completely intact. There will frequently be a basic fascial separation which is easily missed if the operator is not conscious of the problem. If a demonstrable fascial lesion is present, the peritoneum should be incised, the fascial laceration repaired, and the wound closed following the techniques described above.

When the repair has been satisfactorily accomplished, the uterus will be well forward in position, easily maintained without need of further supportive measures. The corpus may be depressed into the cul-de-sac with pressure, but upon release will immediately return to a normal position. As previously described, the uterus will have lost about one-third of its size during the operative procedures, as the marked degree of venostasis so characteristic of this defect is relieved.

For several years, a Gilliam-Crossen type of suspension procedure was added to the technique described above as insurance of adequate uterine support. For the past two years, as experience has taught the effectiveness of the minimal surgical procedure described, no additional suspension techniques have been deemed routinely necessary.

Operative Results

Brief mention should be made at this point of the immediate postoperative results, before presenting the long-range re-evaluation of the patients. There was no mortality in the series. Seven patients were designated morbid during their hospital stay (temperature above 38° C. on other than the day of operation). One patient had persistent urinary retention (the cystocele repair from below) and did not void spontaneously until the fifth day after surgery. One patient suffered a superficial wound infection which drained spontaneously, and healed without further incident. This is a complete list of the immediate untoward postoperative results. All patients were in the best of health at the three months postoperative check.

The patients described in this series have been followed from one to six years. Thus, a satisfactory evaluation of the surgical results obtained is possible from both an anatomical and a clinical viewpoint. All patients in the series were carefully questioned and examined approximately one year after the surgery had been accomplished, to complete the data on this subject.

From a purely anatomical point of view, it can be unequivocably stated that the results of the surgery were completely satisfactory. In all 28 cases the uteri had returned to apparently normal size, and were in a forward position. Motion of the corpus was without restriction in any direction. The "universal-joint" feeling of the cervix had completely disappeared in all cases. As the cervix was moved, compensatory motion was noted in the corpus. The three cases which needed additional perineal support had good postoperative results. The coned cervices (8 cases) were well epithelized and the cervical canals demonstrably patent. All patients were in good health at the time of the one year check examination.

Each patient was then questioned in detail as to her impression of the clinical results obtained from the surgery. The responses have been tabulated (Table V) and are listed hereafter with a discussion of the clinical failures encountered.

TABLE V. CLINICAL FAILURES

SYMPTOMS DESCRIBED	NO. CASES REPORT POSITIVE	NO. CASES OPERATIVE FAILURE*
1. Dyspareunia	24	2
2. Excessive physical fatigue	24	3
3. Dysmenorrhea	22	9
4. Generalized pelvic distress	21	0
5. Specific localization of pelvic distress	19	5
6. Emotional instability	16	3
7. Metrorrhagia	12	1
8. Chronic headaches (occipital)	9	3
9. Menorrhagia	5	0
10. Genitourinary symptoms	5	0
11. Chronic nonspecific vaginal discharge	5	0
12. Premenstrual defecation pain	4	0

*Postoperative failures determined by exhaustive questioning of patients one year after surgery.

1. Dyspareunia.—Two of the original 24 patients who described painful coitus continued to complain of this distress one year after surgery. One of these patients stated that she was still distressed "at times" but that "the situation was infinitely improved over what had previously been the case." (This individual reported a primary dyspareunia on the preoperative questioning.) The second patient had noted no significant relief subsequent to the surgery. This woman was one of the 8 individuals who had a wide cervical conization done. The previously fish-mouthed cervix had been adequately repaired and was well epithelized. In this instance any sudden pressure on

the cervix elicited a very real pain response, but careful motion of the cervix or corpus in any direction was without distress. Although certainly a clinical failure, it is probable that this case is an example of true cervical pain.

2 and 6. Excessive Fatigue and Emotional Instability.—The same 3 patients stated that there had been no notable relief of either of these two primary complaints in their cases. From a purely anatomical point of view the surgical results were excellent. Other primary complaints such as dyspareunia or generalized pelvic distress had been eliminated, but these complaints of emotional instability remained despite a thorough physical and laboratory check. Despite moderate psychosomatic efforts, the poor results have not been satisfactorily alleviated.

3. Dysmenorrhea.—Nine of the 28 patients operated upon continued to have menstrual cramping. Included in this group, however, are the 6 patients whose distress antedated their particular obstetrical misfortune. Thus only 3 of the 16 patients who acquired a significant degree of dysmenorrhea as a part of the "universal-joint" syndrome were unimproved. All three patients were improved as to other basic presenting complaints, but had obtained no relief from menstrual cramping. Nothing further was done for these patients.

5. Specific Localization of Pelvic Distress.—Failure results were reported in 5 of 19 patients with particular symptoms of pelvic distress. One, the patient with the unimproved dyspareunia, complained bitterly of pain associated with pressure on the cervix. The second reported an area of vague distress in the suprapelvic area. Examination was negative other than to elicit a mild but definite pain response. No attempt at therapy was instituted. Three patients reported residual backache which was relatively unimproved after surgery. These patients were placed in the hands of a competent orthopedist who returned a diagnosis of chronic sacroiliac strain for one patient, a suspected ruptured intervertebral disc for the second, and no established diagnosis for the third individual.

7. Metrorrhagia.—Eleven of the 12 patients who complained of metrorrhagia and all 5 of the patients with accompanying menorrhagia reported marked improvement in symptoms. One patient (the curettings showed endometrial polyps) still has flooding with periods and is to have a second curettement.

8. Chronic Headaches.—Three individuals out of an original 9 with a primary complaint of chronic occipital headaches were unimproved subsequent to surgery. Nothing further was done for these individuals.

In closing the long-range postoperative evaluation, brief mention should be made of results noted subsequent to pregnancy, conceived and terminated, after the repair of the "universal-joint" cervix. Six of the 28 patients operated upon conceived and delivered subsequent to the surgery and one of the patients produced twins.

In brief, all deliveries were vaginal and without incident. Expulsive forces during the second stage of labor were observed to be excellent. In all cases, a three months post partum check demonstrated the uterus forward, of normal size, and mobile without distress. There was no return of the symptoms associated with the "universal-joint" cervix in any patient subsequent to her delivery.

Comment

The recognition of the "universal-joint" cervix has delineated a clinical entity to explain in part the multiplicity of complaints and findings described under the inclusive title "Vascular Congestion and Hyperemia." Surgical

correction of the broad ligament lacerations, which are the anatomical basis for the "universal-joint" syndrome, is essentially simple. Postoperative results have been more than satisfactory.

The registering complaints are essentially those described by any individual whose pelvic pathology results in vascular congestion and hyperemia. Acquired dyspareunia (with deep penile penetration), secondary dysmenorrhea, a constant state of semiexhaustion, and a generalized as well as a specific pelvic discomfort constitute the major distress problems. Symptoms of emotional instability recur in direct proportion to the degree of broad ligament laceration, and the elapsed time associated with the present history.

The source of the "universal-joint" cervix is primarily a major obstetrical distress. There is usually either a positive or extremely suggestive history of a misfortune of pregnancy from which to date specifically the onset of symptoms. Such positive histories as severely difficult forceps delivery, breech delivery, precipitous delivery, infant of excessive size, and vaginal packing techniques were encountered in the described series of cases. The suggestive histories of obstetrical distress include such reports as a broken clavicle, fractured skull, spastic infant, etc.

It is important to note that although a patient may be unable to describe an obstetrical misfortune in her past history, she may well be able to date the onset of her "universal-joint" symptoms to a particular delivery. Frequently, the physician in charge of the case will not see fit to describe the particular obstetrical misfortune in detail to the patient or, for that matter, even to mention that he "got into trouble" or that "things didn't go so well."

At pelvic examination, the badly retroverted uterus and the severed feeling of the cervix are constant findings. There is little answering or compensating motion of the corpus when the cervix is moved in any direction. Also of note is the pain response elicited by pressure on the cervix in an upward direction, or pressure on the corpus in the cul-de-sac. The feeling associated with the "universal-joint" cervix may perhaps be best described as akin to the cervical component of an advanced "Hegar's sign" of early pregnancy.

At laparotomy, broad ligament lacerations were constantly encountered. Usually, bilateral in distribution, the lacerations occasionally extended inferiorly through Mackenrodt's ligament to include the sacrouterine ligament. The more widespread the lacerations, the greater the degree of clinical distress encountered. The corpus was always encountered in third-degree retroversion (easily reducible) and demonstrated marked chronic passive congestion. During the pelvic repair component of the "universal-joint" surgery, the corpus frequently lost at least one-third of its size, while being artificially supported in an anterior position.

The ovaries are usually prolapsed with the corpus. This adds to the feeling of general pelvic distress (constant tension on the infundibulopelvic ligaments), and may produce a moderate degree of ovarian failure. It is possible that the frequently encountered complaints of excessive and easy fatigability, emotional instability, and occipital headaches may represent clinical symptoms of ovarian inadequacy. Frequently reported symptoms of menstrual dysfunction

(menorrhagia and metrorrhagia) may also represent a continuation of minimal ovarian failure and/or uterine vascular congestion. The ovaries are usually increased in size (about one-half), and have a cystic tone and tendency. Venous congestion in the infundibulopelvic ligaments was frequently demonstrated.

The interesting phenomenon of free serous fluid present in the pelvis (30 to 80 c.c.) at the time of laparotomy is worthy of conjecture. Free fluid in the pelvis has been described in the past on several occasions. Taylor was particularly concerned with its origin. It is felt that the source of the serous fluid, almost constantly present in the cases of the "universal-joint" cervix, is peritoneal weeping. Lacerations of the peritoneum and of the fascia of the broad ligament cause marked venous congestion due to lack of adequate vessel support. On top of this is the purely mechanical factor of increased pelvic venous pressure associated with the retroverted uterus.

There must be a marked tendency toward extravasation of serum into the pelvic tissues as the result of the advanced degree of venous stasis associated with this syndrome. If the retentive tissues (peritoneal and fascial layers) are deeply lacerated, there is nothing to prevent a slow leakage of fluid into the pelvic cavity. This slow leakage, once actually demonstrated at laparotomy as a slow steady drip, in turn accounts for the concentration of straw-colored fluid noted in the pelvis when the abdomen is opened.

The pelvic viscera and parietal peritoneum are in turn irritated by the concentration of fluid in the pelvis. The serosal surface of the terminal gut and parietal peritoneum are constantly injected and demonstrate the typical capillary enlargement so characteristic of chronic, low-grade irritation and insult. It is felt that the free fluid which leaks from the lacerated broad ligaments is steadily reabsorbed by the multiple peritoneal surfaces. In this manner, the fluid in the pelvis is held to a relatively constant minimum.

The surgical repair of the lacerated pelvic tissues is obviously a simple procedure. Originally an additional suspension technique (Gilliam-Crossen) was employed. Once confidence was gained in the newer repair technique, routine suspension of the corpus was discontinued.

An important point should be made here in regard to the routine suspension techniques that have obviously been used in this situation many times in the past. There is no question but that suspension techniques will help relieve many of the patients with the "universal-joint" syndrome. Many suspension patients, however, continue to complain of pelvic aching and heaviness after routine surgery. Not impossibly, these patients are still draining fluid from their unrepaired lacerations and, as a consequence, continue to present symptoms of chronic pelvic insult. Whether or not one is following previously established suspension techniques, the broad ligaments should always be checked for laceration sites. Many poor postoperative results will be avoided if this precaution is routinely taken in the future.

Postoperative results in the presented series have been generally satisfactory. The acquired dyspareunia and dysmenorrhea, the sensation of extreme fatigue, and the complaints of general or specific pelvic ache are usually

markedly improved or completely alleviated. During the first postoperative week, those patients with a generalized or specific pelvic ache will describe marked or complete relief of symptoms if the surgery has been successfully accomplished. Within three weeks to six weeks, the sensation of excessive fatigue lessens and improvement continues thereafter at a rapid rate. If the first opportunity does not demonstrate marked improvement in the complaint of acquired dyspareunia, the surgical result will not be satisfactory.

The acquired dysmenorrhea usually takes three to six months to reach its maximum recession level. Patients should be warned that usually the first and frequently the second regularly recurring menstrual periods post surgery may be complicated by heavy bleeding or even flooding, even if metrorrhagia has not been one of the presenting complaints. This is due to the anterior positioned and still excessively enlarged uterus, slowly recovering from its advanced degree of chronic passive congestion. Once the uterus completes its involution to normal size (three months at the most), the bleeding complaints disappear.

It frequently takes from three to six months for the ovarian function to return to normal. Complete vaginal cornification is accomplished four to five months postoperatively. The chronic occipital headaches disappear about the time that the excessive fatigability is no longer an issue. There is also a concomitant return to satisfactory emotional balance once ovarian stability has been achieved.

From the limited experience derived from this series, the patient's contemplation of future pregnancy should be stimulated rather than discouraged. Results in this direction in patients previously operated upon for the "universal-joint" syndrome have been completely satisfactory.

Summary

A series of 28 cases has been presented in detail to illustrate the syndrome of the "universal-joint" cervix. A complete evaluation has been recorded of the presenting complaints, history of associated obstetrical misfortunes, and pelvic pathology encountered at laparotomy. The simple surgical detail necessary to alleviate symptoms has been described and pictured. Finally, a detailed postoperative evaluation of results obtained concludes the study.

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THE CURE OF UTERINE PROLAPSE WITH SPECIAL REFERENCE TO THE MANCHESTER OPERATION*†

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THE choice of treatment for cure of uterine prolapse in the absence of uterine disease is controversial. At present it seems that differences of opinion exist not merely between individual gynecologists, but that they also have a geographical distribution. This latter may be accounted for in many instances by the varying percentages of pathological conditions existing in different countries and certainly by the influences which control the frequency and number of pregnancies. There is universal agreement that the condition of uterine prolapse should be treated by vaginal operation, but the controversy lies in whether or not to remove the uterus, particularly in women who have reached or passed the menopause. If in addition to prolapse there is some abnormal uterine condition, it is generally agreed that removal of the uterus is indicated.

This communication is mainly concerned with uterine prolapse and its cure by the Manchester operation. The history of the evolution of the operation is too well known to be recounted here but various plastic operations on each vaginal wall separately and then on both together finally culminated in the operation that we know today.

Before embarking on any operative procedure it is important to try to estimate what should be the ultimate result. A successful operation should fulfill four requirements: (1) cure the prolapse; (2) completely relieve the patient's symptoms; (3) restore the patient's condition so that coitus can be as satisfactory to both partners as it was prior to the onset of the prolapse; (4) not make conception and parturition more difficult.

To achieve these aims, the vagina should be as normal as possible in length, diameter, and mobility.

The Manchester operation consists of anterior colporrhaphy, amputation of the cervix, shortening and stitching of Mackenrodt's ligaments to the front of the cervix, and colpoperineorrhaphy. The whole principle depends on the preservation of the uterus so that its main supports, namely, Mackenrodt's ligaments, can be shortened and stitched to the front of the cervix with the result that, besides keeping the uterus in the upper part of the vagina, the cervix is kept anteverted and the body of the uterus anteflexed. Critics hold that the resultant scarring of the cervix interferes with conception and parturi-

*This study was carried out in the Department of Gynecology, Dr. Steevens' Hospital, Dublin, Ireland.

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tion and that the vagina becomes a rigid channel. The answer to such criticisms is that if the cervix is healthy the surgeon need not amputate but can carry out all the other steps of the Manchester operation. If the patient is young and there is little cervical hypertrophy, then only a small portion need be removed. If after the operation is performed there should be some recurrence of vaginal prolapse caused by another pregnancy, it is not a great ordeal for the patient to have still further repair which will be less extensive than the original operation. The inexperienced gynecological surgeon may excise too much vaginal epithelium, which tends to take away the elasticity and mobility of the vagina. Each stage can be carried out and a successful result accomplished even if it appears at the time of the operation that there is redundancy of vaginal epithelium. The old idea that the success of the operation depends on replacing the vaginal epithelium with scar tissues is now happily of only historic interest. Coexisting lesions such as urethrocele can be corrected in the operation. Leyland Robinson[1] has shown that the cosmetic and functional results are satisfactory, by making a simple variation in the lower part of the incision behind the urethra, making it "U" instead of "V" shaped and closing it in a "T" shape.

At the International and Fourth American Congress on Obstetrics and Gynecology, Te Linde[2] brought to notice the usefulness of the Spalding-Richardson operation. In reporting 400 cases he said: "We believe the procedure has the advantage of vaginal hysterectomy in getting rid of the neoplastic potentialities of the cervix and corpus of the uterus. It has a further advantage of preserving the isthmus of the uterus with good blood supply to which various structures may be attached."

I have done this operation in a small number of postmenopausal patients with uterine prolapse and small fibroids, and I feel that it has a place among the operative procedures for uterine prolapse in selected cases.

A surgeon will make certain modifications in any standard operation during the performance of which he will use his own technique. In the Manchester operation, for example, the scalpel is often used instead of the scissors, a midline incision on the anterior vaginal wall instead of the classical Fothergill, while others use a different technique for tying and stitching Mackenrodt's ligaments. Suture material has always been a contentious issue, and even today the absorbable materials are not without reaction. The vagina is often inhabited by pathogenic bacteria and first-intention healing does not always take place, so that secondary hemorrhage occasionally occurs. For these reasons, the use of a nonabsorbable material such as nylon in suturing the cervix and vagina has many advantages. There is little difficulty in its removal provided no attempt to do so is made for at least six weeks after the operation. If the removal of the stitches is likely to upset the patient, chromic or iodized catgut should be used.

When discussing the importance of the uterus in relation to the operative cure of prolapse, some consideration of the psychological aspects of its presence or absence must be considered. In women past the menopause, the uterus is

of little importance, but in younger women, the question merits attention. Even if further pregnancies are not contemplated, we do not fully realize the impact on the body and mind of removal of the uterus. A sense of frustration may result and the vagaries of human nature are such that another child may be wanted at a later date. We still do not know the effect on the husband of the hysterectomized wife, though in these days of such free removal of the uterus, there is ample material available for study.

There have been very few references by the psychiatrists to the effects of removal of the uterus. Lewis and Jackson[3] were unable to draw any statistical conclusion or inference from the comparative study of 25 castrated women with 42 following hysterectomy. The only other pertinent reference which I have found is in the work of Lindemann,[4] who discovered that restlessness, agitation, and preoccupation with depressive thought content were much more frequent following pelvic operations than after cholecystectomies. The age of the 51 patients investigated by him ranged from 20 to 55, so that many of them were menopausal, which reduces the value of his observations.

The use of pessaries in the treatment of uterine prolapse during the child-bearing years is widely advocated by many practitioners, particularly in countries where the limitation and spacing of children is prohibited. If there are symptoms of prolapse they can be cured by operative treatment and psychologically the patient will be better adjusted. There can be little doubt that pessary treatment during the best years of a mature woman's life must be demoralizing, but with the refinements of modern vaginal plastic operations, fortunately, the pessary is found more frequently in the cupboard than in the vagina.

The synergistic action of the hormones is now accepted, and their inter-relationship is possibly short-circuited by the removal of the uterus, so that besides the vascular effects on the ovary, which may diminish the potency of hormone activity, there may be certain other changes as well. For example, there is also some evidence that a menstrual toxin is secreted by the endometrium and takes part in the menstrual cycle. Are we sure that there are no other substances secreted by the uterus which are of some value to the general well-being of the normal premenopausal woman? If we agree that there is no justification for the removal of the prolapsed uterus in premenopausal women, can we apply the same reasoning to those past the menopause? Furthermore, is the same operative procedure suitable for both age groups? I believe that the Manchester operation modified for patients of different ages and different degrees of prolapse fulfills the requirements in nearly every type of case.

High rectocele and enterocele are occasionally concomitant with uterine prolapse. When these conditions are present it is necessary to stitch the ilio-coccygeus part of the levator ani muscles together from high up in the vagina, sometimes approximating them to the back of the uterus. If there is enterocele, it is important to open up the prolapsed portion of the pouch of Douglas, and to remove the redundant part of the sac; this is then followed by a procedure similar to that for high rectocele. If the uterosacral ligaments are well de-

veloped, they can be approximated before repair of the posterior vaginal wall is done. Rarely is the abdominal approach necessary for the cure of enterocele, and the value of the Spalding-Richardson operation for the cure of this condition has already been discussed.

A consecutive series of cases operated on for uterine prolapse by the Manchester operation will now be presented. The period covered was from the beginning of 1938 to the end of 1951, and the follow-up examination was made at the end of 1952. The total number of Manchester operations performed was 190 and, despite very appealing letters, only 62 of these patients returned for further interrogation and examination. This may appear to be a very small number, but in Ireland it is exceedingly difficult to persuade women to return to the hospital for examination if they are feeling well. Investigation by means of a questionnaire would probably have brought a greater number of cases under review but proper assessment cannot be made without personal interrogation and a full pelvic examination. The length of time that elapsed between the date of the last operation performed in 1951 was twelve months, and the maximum period twelve years. The patients were all examined by me so that there is minimal variation in the interpretation of the results.

TABLE I. AGE GROUP AT TIME OF OPERATION (190 CASES)

AGE	NO. OF PATIENTS
21-30	11
31-40	55
41-50	54
51-60	38
61-70	27
71-80	5
Average age, 47.3 years	
Total	190

Table I shows the age groups at the time of operation. As would be expected, the greatest number of patients were between the ages of 31 and 50 years. In the series under 30 years of age, there were 11 cases, and over 70 years there were 5 cases. Operation is not contraindicated in a fit woman over 70 years of age, the convalescence is easy, and the results are good. It is important, however, that the general condition should be carefully assessed before operation.

TABLE II. AGE GROUP AT TIME OF FOLLOW-UP EXAMINATION (62 CASES)

AGE	NO. OF PATIENTS
21-30	0
31-40	14
41-50	19
51-60	9
61-70	14
71-80	5
84	1
Average age, 52.2 years	
Total	62

The 84-year-old patient shown in Table II was 76 at the time of the operation and prolapse had been present for some 20 years. She doubted the wisdom

of having an operation but when she was told that she was very fit for her age and that she might have another 20 years to live, she consented. She exclaimed when she returned for examination 8 years later, "God bless you, Doctor, I have got the first 8 years off my chest out of the 20 which you promised me and I feel wonderful."

TABLE III. NUMBER OF PATIENTS WHO CONCEIVED AFTER OPERATION (14)

No. of patients who conceived	14	
No. of living children	13	(10 patients)
No. of premature stillborn infants	1	
No. of abortions	11	(9 patients)
No. pregnant at time of examination	3	

The number of patients who conceived after the operation was 14 out of the 62 subsequently examined. There were 33 women in the childbearing age so that the conception figure following the operation was 42.4 per cent. Table III also shows details of the pregnancies and it will be noted that the abortion rate is relatively high.

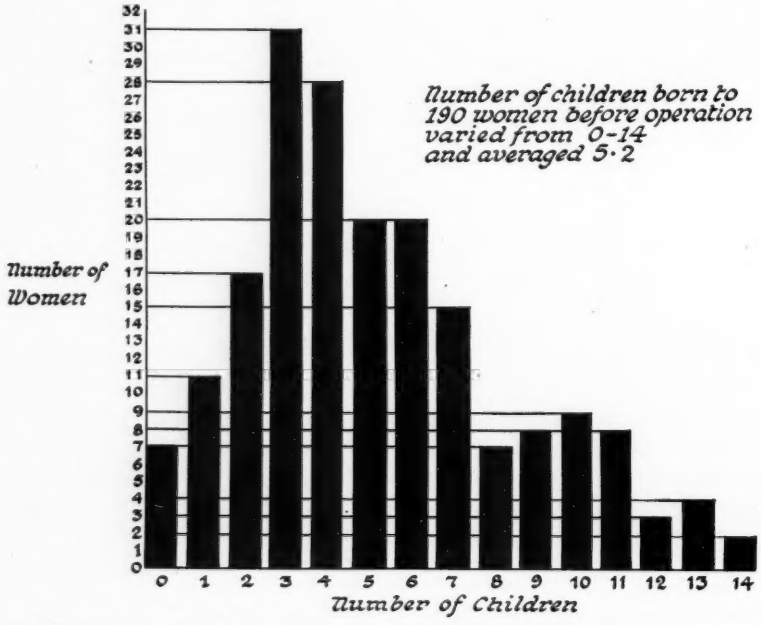

Fig. 1.—The number of children born to 190 women before operation varied from 0 to 14 and averaged 5.2.

The number of cases in relation to parity at the time of operation is shown in Fig. 1. As would be expected, the greatest number operated on were women who had 3 or 4 children. It will be noted that the operation was performed on 7 (3.6 per cent) nulliparous women which is a comparatively high figure and may account for the relative frequency of prolapse in women who have had children in Ireland. Several hypotheses can be advanced as possible causes for this and it is interesting to speculate as to whether faulty diet, which is common in Ireland, may have an influence on the resilience of connective tissue throughout the body.

The pleasure of sexual intercourse was unchanged by the operation in 46 cases (74 per cent) and was not so satisfactory in 9 cases (14 per cent).

There was no case of actual dyspareunia in these 9 cases so that the increased coital discomfort might be ascribed to the wear and tear of marriage.

TABLE IV. RESULTS OF OPERATION: MARITAL RELATIONSHIP AFTER OPERATION

Operation made no change	46
Operation increased discomfort	9
Widowed	7
Total	62

TABLE V. RESULTS AFTER OPERATION

	SYMPTOMS	HAD CHILDREN
None	45	7
Slight	12	2
Moderate	5	1
Total	62	10

Symptomatic relief is most important following any operation especially in a condition such as uterine prolapse. There were 17 women who were not completely cured of their symptoms and, of these, the results in 5 could be classified as unsatisfactory, the remaining 12 patients having very slight discomfort.

It is interesting to note that stress incontinence of urine was not a feature in any of the 62 cases examined either before or after operation.

TABLE VI. CONDITION AFTER OPERATION*

CONDITION ON EXAMINATION AFTER OPERATION		SUBSEQUENTLY HAD CHILDREN (10 PATIENTS)
No abnormality	21	1
Very small cystocele	24	4
Cystocele	10	3
Small rectocele	8	4
Deficient perineum	3	3
Eroded cervix	1	1

*Some patients are included in more than one category.

TABLE VII. FOLLOW-UP EXAMINATION

TOTAL	NO SYMPTOMS	WITH SYMPTOMS
62	45 (72 PER CENT)	17 (28 PER CENT)

SYMPTOMS	CONDITION	CHILDREN AFTER OPERATION
1. Slight backache	Small cystocele	0
2. Pressure	Cystocele	1
3. Pressure	Small cystocele and rectocele	1
4. Frequency	Moderate cystocele	0
5. Slight backache	Normal	2 abortions
6. Vulvar discomfort	Small cystocele	0
7. Vaginal discomfort	Small cystocele	0
8. Lower abdominal discomfort	Slight perineal deficiency	2
9. Slight vaginal discomfort	Deficient perineum	0
10. Irregular menstruation	Cystocele	0
11. Vulvar irritation	Vulvovaginitis	0
12. Slight leukorrhea	Normal	0
13. Lower abdominal discomfort	Normal	0
14. Vulvar irritation	Leukoplakia, malignant-vulvectomy	0
15. Slight dysmenorrhea	Normal	0
16. Pressure	Cystocele, moderate	2 abortions
17. Slight pressure	Very small cystocele	0

The condition most likely to recur after operation is cystocele which is not necessarily due to subsequent confinement. It will be seen that this did occur in 10 patients and was sufficiently large to be called pathological. The 24 cases of very small cystocele are of no significance and were symptomless.

It might be expected that some cervices would become unhealthy or that uterine descent might occur but neither of these complications was seen. It seems, therefore, that cystocele is the most likely condition to recur after this operation performed by my technique. This bears out the well-known fact that cystocele is not dependent on uterine prolapse and is often the most difficult part of genital prolapse to cure. My technique for this part of the operation is to sew the pubocervical fascia and the vaginal epithelium separately, using a continuous stitch.

The final and very important issue to be discussed in the treatment of prolapse is whether the uterus should be removed in every case past the menopause to prevent the possibility of subsequent uterine cancer. The Manchester operation has found favor in Dublin because of the very small risk in this respect, and is the operation of choice in the majority of cases as the results have been good. For instance, in the 10,000 patients who attended the Gynaecological Out Patients' Department of Dr. Steevens' Hospital from the beginning of 1937 to the end of 1952, there were 14 who had carcinoma of the body of the uterus—an incidence of 0.16 per cent, and it so happened that not one of these cases was associated with uterine prolapse either before or after operation. This Out Patients' Department is fairly typical of Dublin. The clientele would be fairly representative of the city and therefore the figure for the incidence of carcinoma already given is a fairly accurate random sample.

In conclusion, it appears that the main question at the present time in the treatment of uterine prolapse is the value of the uterus itself. The great advances in all branches of surgery, together with the dexterity of the modern operating gynecologist, may be leading to overenthusiasm and a more radical approach to the treatment of prolapse than is really necessary or advisable. Possibly the time has come once again to evaluate this important issue and to decide whether the operation devised some 60 years ago has maintained its position as a panacea for the treatment of prolapse when the uterus is healthy.

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REAPPRAISAL OF THE DIAGNOSIS IN UTERINE SARCOMA

Review of Forty-Nine Cases

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SINCE the first report of sarcoma of the uterus by Carl Meyer in 1860, it is evident that the only consistent findings in succeeding reports are the difficulties in diagnosis, pathologic as well as clinical, disagreement as to classification, and the generally poor end results. Novak and Anderson, Evans and Kimbrough independently tried to establish methods of diagnosis by using the number of mitoses present as a measure of the malignancy. Bosse and Stanton showed in their series of cases that the degree of invasiveness, gross or microscopic, was very closely correlated with the subsequent clinical course. In reviewing sixteen cases of sarcoma of the uterus Murray and Weitzner state that they agree with "Corscaden and Stout, and McFarland, that before the diagnosis of sarcoma of the uterus is made, the histological interpretation must be supported by clinical findings, such as rapid growth, evidence of infiltration, metastasis, and recurrence."

Because of these discrepancies and difficulties it is felt that reports of this disease, even though based on relatively small numbers of cases, are worth while. Kimbrough reported 43 cases, Novak and Anderson 51 cases, Randall 39 cases, Thornton and Carter 24 cases, Finn 33 cases, MacFarlane 42 cases, and there are many other reports of small groups of cases.

The material for this communication is based upon a restudy of 49 cases originally diagnosed by the Department of Laboratories of this hospital as nonepithelial malignancies of the uterus. The material was obtained during the years 1937 through 1952. The original diagnosis was some form of sarcoma in 48 instances and hemangioendothelioma in one instance. All microscopic material was reviewed and in many instances the original blocks were recut and special staining techniques employed.

Table I illustrates the differences between the original pathologic diagnosis and the final diagnosis in those cases where the diagnosis of sarcoma was confirmed. The unclassified tumors were felt to be histologically malignant and nonepithelial, but were listed as unclassified because no further definitive statement regarding them could be made. Finn, Thornton and Carter, and others have reported nonclassifiable tumors of this type.

Table II lists those cases which were rediagnosed as either benign lesions or as epithelial malignancies of the uterus. The majority of the misdiagnosed cases occurred in those tumors originally reported as showing sarcomatous changes within leiomyomas.

TABLE I. FINAL DIAGNOSES

FINAL DIAGNOSIS	NO.	ORIGINAL DIAGNOSIS
Endometrial sarcoma	2	1 endometrial sarcoma 1 mural sarcoma
Mixed mesenchymal sarcoma	5	1 mural sarcoma 2 endometrial sarcoma 2 carcinosarcoma
Rhabdomyosarcoma	1	Leiomyosarcoma
Carcinosarcoma	3	2 carcinosarcoma
Collision type 2 True carcinosarcoma 1		1 carcinosarcoma coincident
Primary mural	8	6 mural sarcoma
Spindle 4		1 carcinosarcoma
Mixed 4		1 secondary sarcoma
Secondary sarcoma in leiomyoma	6	3 mural sarcoma 3 secondary sarcoma
Unclassified	4	2 mural sarcoma 2 secondary sarcoma
Total	29	

TABLE II. CASES MISTAKENLY DIAGNOSED AS SARCOMA

REDIAGNOSIS	NO.	ORIGINAL DIAGNOSIS
Inflammatory polyp	1	Secondary sarcoma
Stromatous endometriosis	1	Hemangioendothelioma
Myoma	12	Secondary sarcoma
Cellular 8		
Degenerating 4		
Material insufficient for diagnosis	1	Primary sarcoma
Adenocarcinoma anaplastic	3	Carcinosarcoma
Anaplastic carcinoma of cervix	1	Primary sarcoma
"Myoblastoma"	1	Secondary sarcoma
Total	20	

Wheelock and Warren reported 113 cases of leiomyosarcoma of the uterus which they regarded as clinically benign. We feel certain that some of our rediagnosed cases fall into this group. Davis, Howe, and French group their cases into leiomyosarcoma and low-grade leiomyosarcoma. This is based on the same difficulties in diagnosis.

After rediagnosis of the 12 cases as benign myomas, the clinical histories and follow-up studies were reviewed. We did not refer to the clinical records until the final studies were made on the pathologic material. The 12 cases we rediagnosed as benign myomas were reclassified as cellular myomas (Fig. 1) in 8 cases and myomas with degenerative changes (Fig. 2) in 4. One patient was lost to our follow-up. Of the 11 remaining cases, 2 have been seen for seven years, 2 six years, one five years, 3 actively followed four years, and 3 patients followed for three years. None of the patients followed have shown any evidence of previous malignant disease in the way of local recurrence or distant metastases. This would preclude designation of any of these cases as "myoma malignum" as described by Ewing.

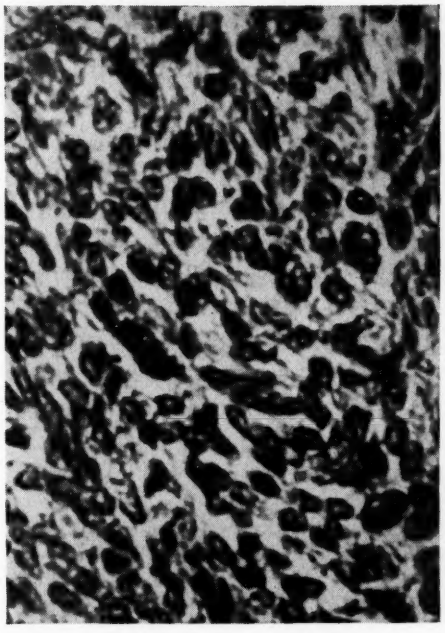


Fig. 1.—Cellular myoma. Originally called "leiomyoma with sarcomatous changes." Diagnosis changed to benign lesion because of uniformity of nuclei despite cellularity. (×60; reduced ¼.)

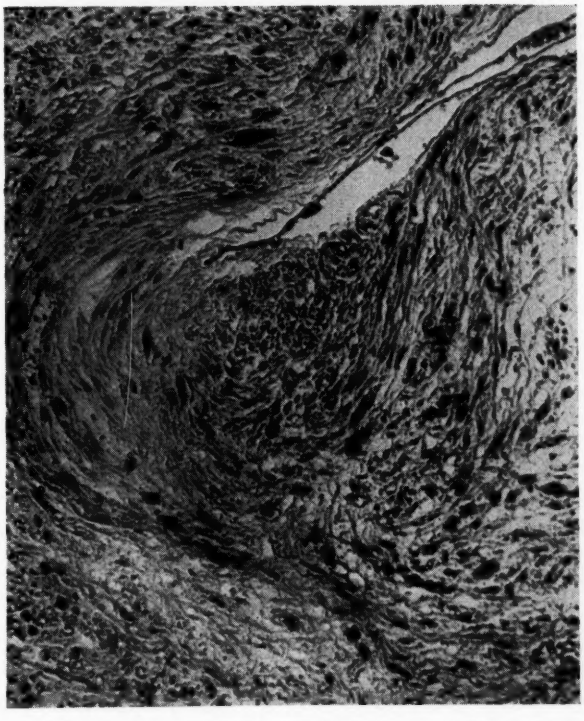


Fig. 2.—Myoma with degenerative changes. Originally called "sarcomatous degeneration." Atypical cells are found only in area of edema. (×300; reduced ¼.)

There were 3 very debatable tumors among the group rediagnosed as benign, one of which we called an inflammatory polyp of the uterus following radiation and pyometra. The second we diagnosed as stromatous endometriosis, and the third is a case we designated as "myoblastoma," because of the general appearance of benignancy of this tumor as well as the very early cell type present. All 3 of these patients are alive and well after their surgery, with no evidence of metastases. These cases will be discussed in more detail in the section on pathology. Pedowitz, Felmus, and Grayzel, in studying vascular tumors of the uterus, designated the first two of these tumors as hemangiopericytoma. Greene and Gerbie in a recent work reported 5 cases of hemangiopericytoma of the uterus. The difficulty and incomplete accord with this diagnosis are brought out by their reporting a case previously reported from the same clinic as endometrial sarcoma; the patient, however, later died of diffuse carcinomatosis.

In the further rediagnosis of sarcoma to nonsarcoma, there were 4 anaplastic carcinomas, 3 endometrial and one spindle-cell carcinoma of the cervix.

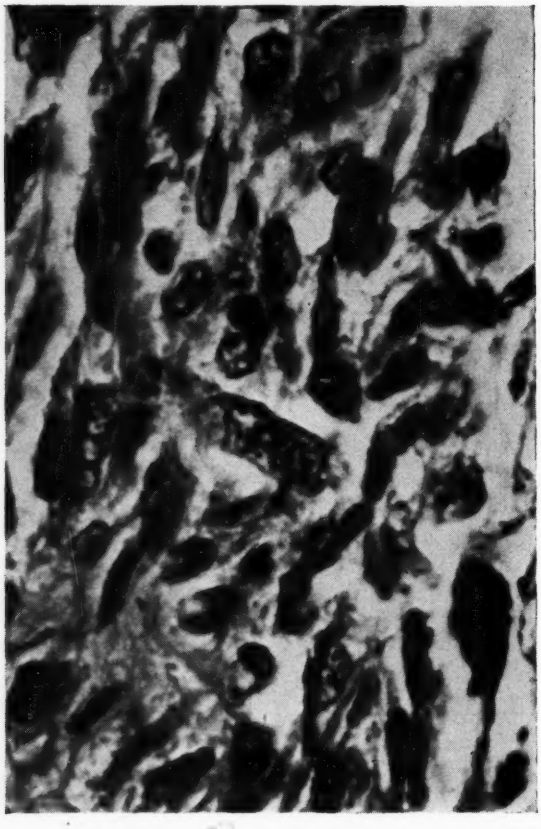


Fig. 3.—Leiomyosarcoma, primary. (×600; reduced ¼.)

Pathologic Features

In this series of cases little or no difficulty was encountered in separating the tumors of endometrial origin (Fig. 14) from those developing within the myometrium proper (Fig. 3) or from within a leiomyoma (Fig. 4). The gross

description was often, in itself, a clue, as the endometrial sarcomas generally produced a multipolypoidal, necrotic, and bulky intracavitary mass. The mural tumors in this series did not involve the endometrium to any significant extent.

The greatest difficulty in the nonendometrial cases involved the decision as to whether or not the histologic features warranted a bona fide diagnosis of malignancy. In this portion of the study four histologic features were primarily considered; pleomorphism, mitoses, cellularity, and the presence of giant cells. If all features were present the tumor was unhesitatingly called sarcoma. The presence of cellularity alone was not considered sufficient for the diagnosis of sarcoma and many of the tumors studied (originally diagnosed as sarcoma or "sarcomatous changes") fell into this category. Because of the lack of pleomorphism in these examples, the cases were rediagnosed as cellular or highly

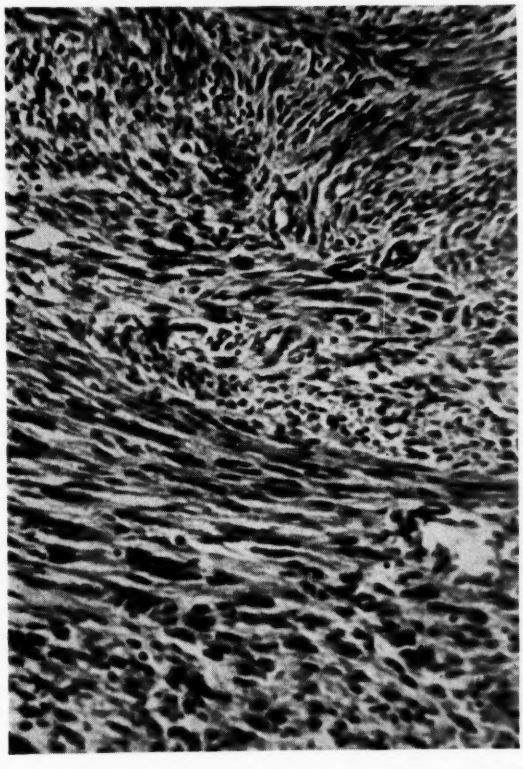


Fig. 4.—Leiomyosarcoma, secondary. (×300; reduced ¼.)

cellular leiomyomas. In several instances cellular, but nonpleomorphic foci were present in otherwise ordinary, benign leiomyomas; the diagnoses in these instances were also revised from "leiomyoma with sarcomatous changes" to "leiomyoma with focal cellularity." The misinterpretation of cellularity as sarcoma accounted for the misdiagnosis of 8 cases and was by far the largest cause of error. Almost half of the tumors which we felt to be benign, despite a previous report indicating sarcoma, were misdiagnosed because their cellularity was mistaken for malignancy.

In 2 of the tumors that answered to the gross description of leiomyomas the previous diagnosis of "sarcomatous change" had apparently been rendered solely upon the presence of cells with elongated nuclei that stained deeply. Upon restudy it was apparent that these cells occurred only in areas of edema and appeared to represent the effects of a degenerative rather than a neoplastic process. We found no instances in which giant cells alone constituted the only presumptive evidence of malignancy. When present, sufficient nuclear pleomorphism and cellularity coexisted so that a histologic diagnosis of sarcoma was felt to be tenable.

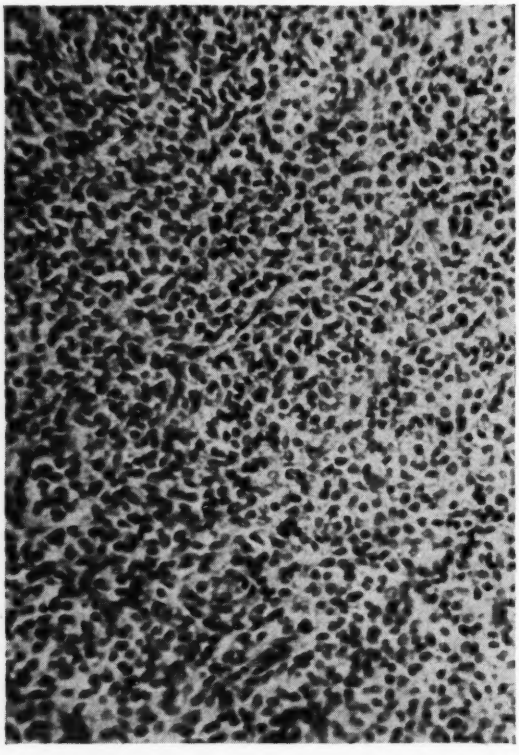


Fig. 5.—Sarcoma unclassified. Recurrence three years after local excision. Patient alive and well five years after hysterectomy. (×300; reduced ¼.)

When we felt the diagnosis of sarcoma was justified, an attempt was made further to subdivide the lesion on a histogenetic basis. This we soon saw was possible only in a minority of instances. We were often unable definitely to describe a spindle-cell sarcoma as fibrosarcomatous or leiomyosarcomatous.

The tumors composed of rounded cells offered even greater difficulties. Here we were confronted with the problem of deciding whether the cells represented immature smooth-muscle cells, hemangiopericytes as described by Stout and Murray and Stout, stromal cells, or undifferentiated mesenchymal cells. The first (Fig. 5) occurred in a 27-year-old girl upon whom local excision of a mural tumor was performed. This tumor was composed primarily of small spindle cells. The pathologist's diagnosis was leiomyoma, although there was

little resemblance of the tumor cells to smooth-muscle cells. Recurrence was present three years later and this time a total hysterectomy and bilateral salpingo-oophorectomy were performed. The tumor now consisted of round cells that were closely packed together. A slight to moderate degree of pleomorphism was felt to be present. The tumor was now reported as a secondary leiomyosarcoma. The pathologic diagnosis submitted upon our restudy was "sarcoma unclassified." In this instance we cannot with any degree of certainty classify this tumor as either a low-grade sarcoma of poorly differentiated smooth-muscle cells, or mesenchymal cells. This patient is alive and well five years after hysterectomy. This case has been reported as hemangiopericytoma along with

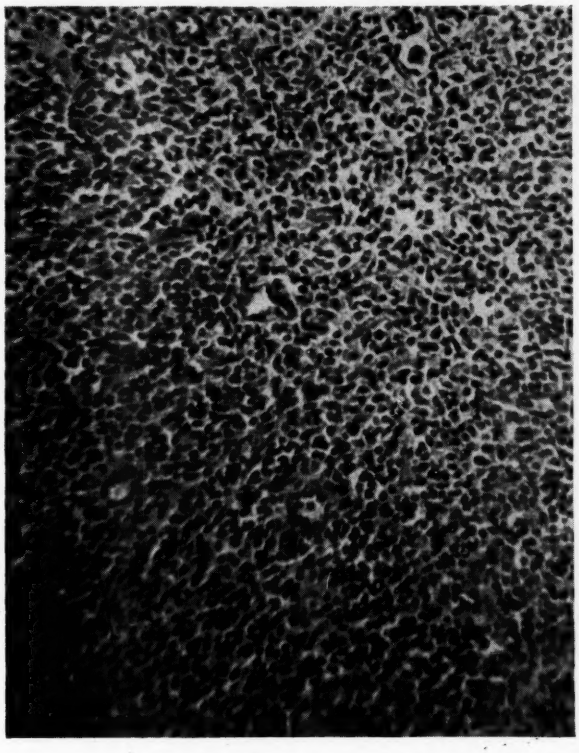
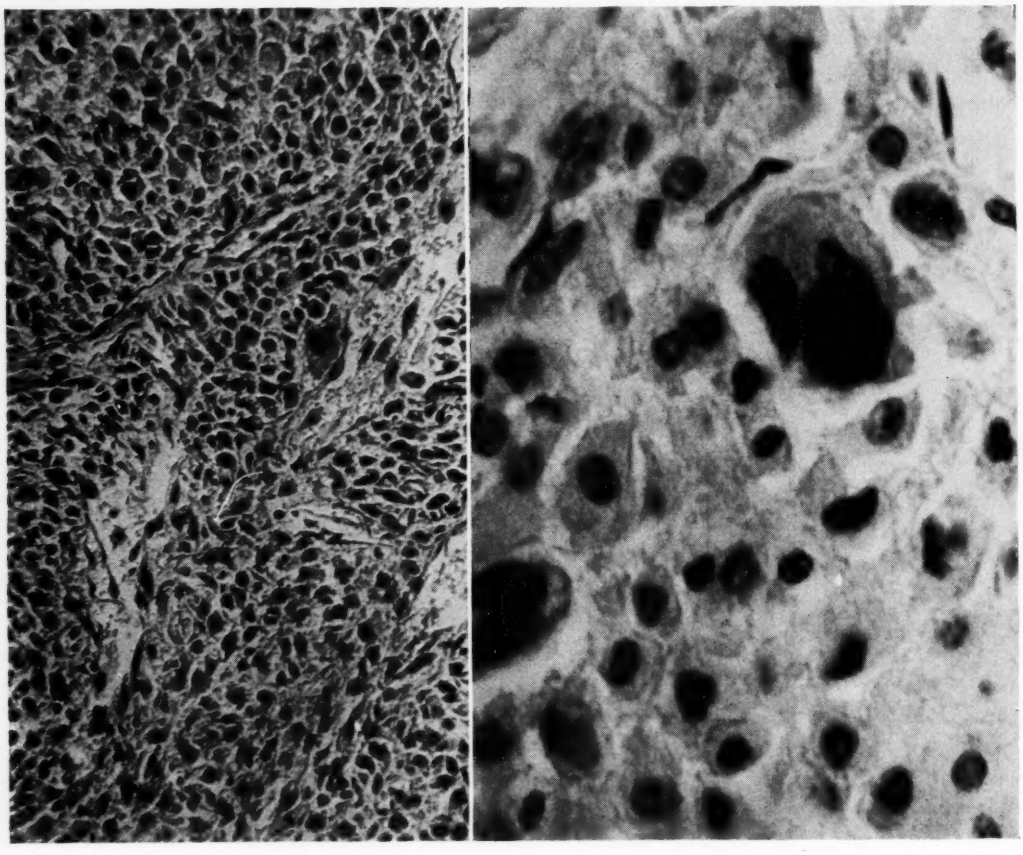


Fig. 6.—Sarcoma unclassified. Composed of small cells and occasional large eosinophilic cells. Metastasized to lungs. (×300; reduced ¼.)

the cases mentioned previously. Our own feeling is that this case might represent a hemangiopericytoma; because of our own doubts, however, as well as the doubts of several other pathologists, we prefer to carry this tumor as unclassified at the present time.

The second instance (Fig. 6) occurred in a 53-year-old patient who had a large, encapsulated, hemorrhagic, and cystic mass attached to the fundus of the uterus by a distinct pedicle. It was composed of small cells with deeply staining nuclei and occasional widely separated larger eosinophilic cells. The suggested diagnoses of this tumor were granulosa-cell carcinoma arising from a bipartite ovary and sarcoma probably arising from immature smooth-muscle

cells. This patient died soon afterward with pulmonary metastases. Langley, Smith, and Woodcock reported a similar tumor which they designated as granulosa-cell tumor of the uterus. The cells in the tumor they described reproduced a cordlike pattern lacking in our case. Furthermore, our tumor additionally contained large eosinophilic cells, which suggest a myogenic origin.

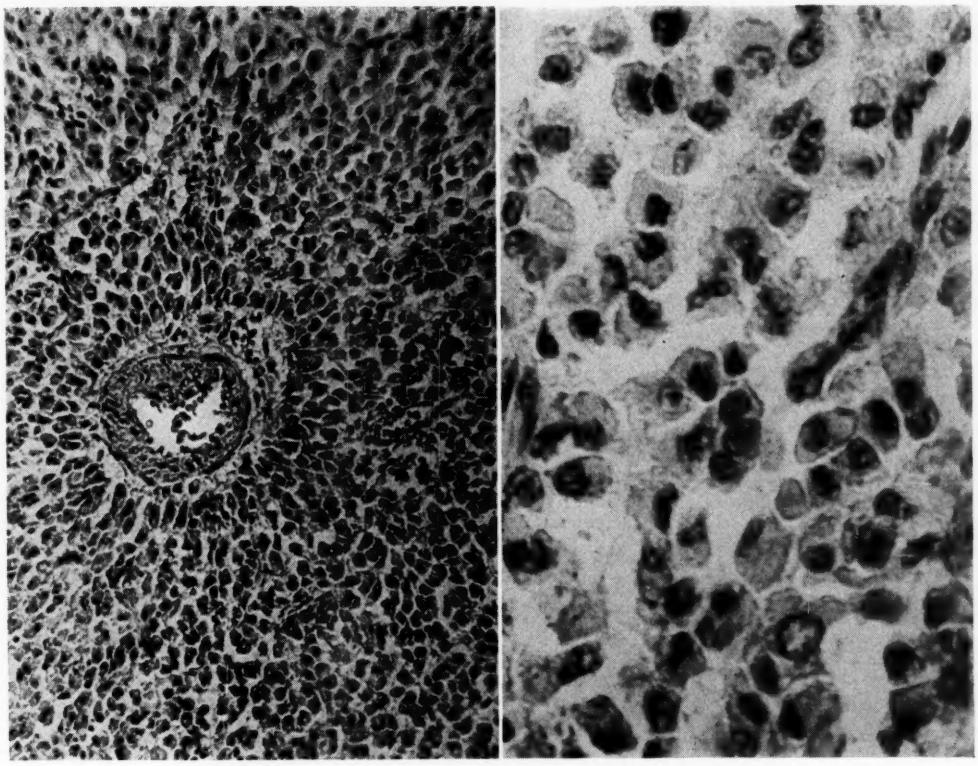


A. *B.*

Fig. 7.—*A*, Sarcoma unclassified. Previously called leiomyosarcoma. Tumor consists of eosinophilic cells and occasional giant cells. (×300; reduced ¼.)
B, High-power view of Fig. 7, *A*. (×600; reduced ¼.)

The third tumor (Fig. 7), also in the unclassified group, was composed of moderate-sized eosinophilic ovoid cells with small, round, deeply staining nuclei and giant cells. This tumor was of large size and the patient is alive and well 16 years after hysterectomy. In spite of the clinical benignancy of the tumor, it was definitely malignant histologically. We feel also that this case is related to the second case previously described in the unclassified group. The common ground seems to be in the eosinophilic cells which predominated in the third case, and were significantly present in the previously described case, in addition to the predominant small, round type of cell. These eosinophilic cells may be a form of immature muscle cells and also remotely suggest an early phase in the development of rhabdomyosarcoma. No cross striations were found in these

two tumors, although there was a suggestion of strap cells present. Also encountered in this series was a tumor composed of a similar type of eosinophilic cell in which no malignant features were noted. This tumor (Fig. 8) appears in our classification as benign "myoblastoma." The patient is alive and well seven years after hysterectomy.



A. *B.*

Fig. 8.—*A*, "Myoblastoma." Previously called myogenic sarcoma. Tumors composed of eosinophilic cells. Note radial arrangement about blood vessel. Note resemblance to Fig. 7, *A*. (×300; reduced ¼.)

B, High power of Fig. 8, *A*. (×600; reduced ¼.)

The fourth unclassified tumor (Fig. 9) was placed in this group because of the presence of an architectural pattern featured by the regimentation of small, uniform, dark-staining nuclei into "palisades." The regimentation of nuclei was suggestive of that seen in neurinomas, but one of us (S. A. W.) recalled the regimentation feature as characteristic of "myochyme" or embryonic smooth muscle as described in Henke-Lubarsch. Due to the lack of knowledge concerning the behavior of this type of tumor, it was decided to place it in the unclassified group. This patient is living and free of disease ten years after vaginal hysterectomy.

Of the endometrial tumors, 4 were rejected as sarcomas upon restudy as they were felt to be carcinomas, 3 of anaplastic endometrial type and one a spindle-cell carcinoma of the cervix. In one of the cases the material submitted for examination was considered by us to be insufficient for a diagnosis, although

malignancy was present; we could not tabulate this case as a sarcoma. Of the remaining 13 cases in the endometrial group, it was necessary to revise the diagnosis of malignancy to benignancy in only 2 instances. These deserve further comment.

One tumor (Fig. 10), previously diagnosed as hemangioendothelioma in 1942, was included in this series because the term "hemangioendothelioma" implies a nonepithelial malignant tumor. Review of the sections taken and comparison with lesions previously reported establish this as one of "stromatous endometriosis" or "stromal myosis," as described by Frank, Park, Henderson, Hunter, and others. Other examples of this entity have been regarded in the

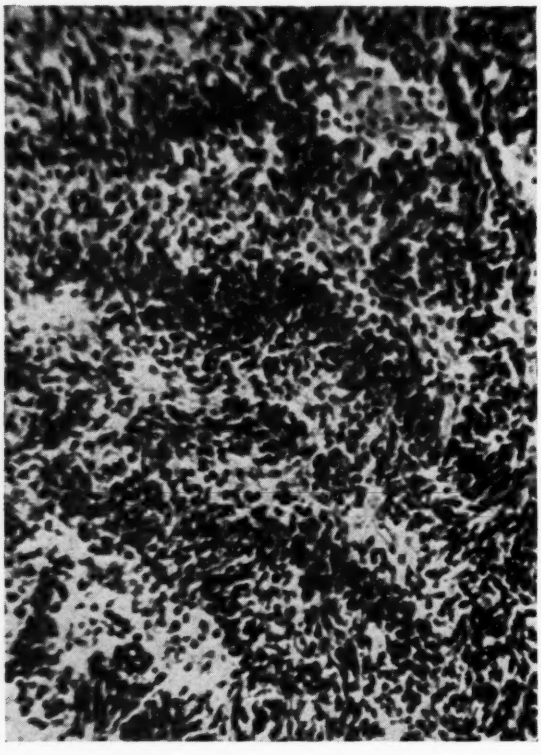


Fig. 9.—Sarcoma unclassified. Note palisading of nuclei. (×300; reduced ¼.)

past as either sarcoma of the endometrium or as a tumor of vascular origin, as in this instance. To justify this assumption one need only look at the description and photomicrograph of the case reported by Kotz and Kaufman in 1938, under the heading of sarcoma of the uterus, and the comments of various authors who have described examples of this condition. Within the past year, 2 other examples of "stromal myosis" have been seen in this hospital, but since neither was diagnosed as sarcoma they are not included in this series.

Another instance (Fig. 11) in which the original diagnosis of an endometrial tumor was changed from one of malignancy to one of benignancy occurred in a 71-year-old patient with pyometra and a bulky, necrotic intracavitary tumor. This tumor was diagnosed originally as a leiomyosarcoma. Upon restudy, the mass was seen to be composed, from within outward, of a zone of necrosis, a

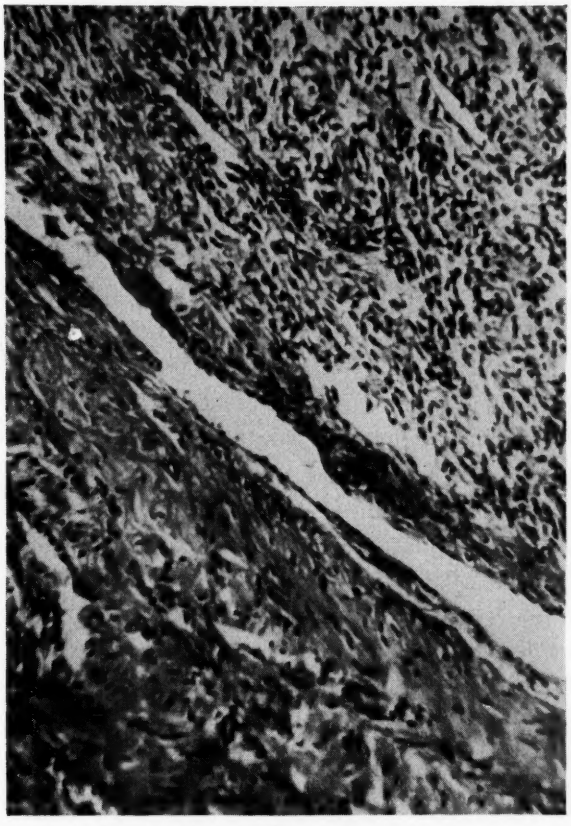


Fig. 10.—High-power view of stromatous endometriosis, showing space between myometrium and stromal tissue.

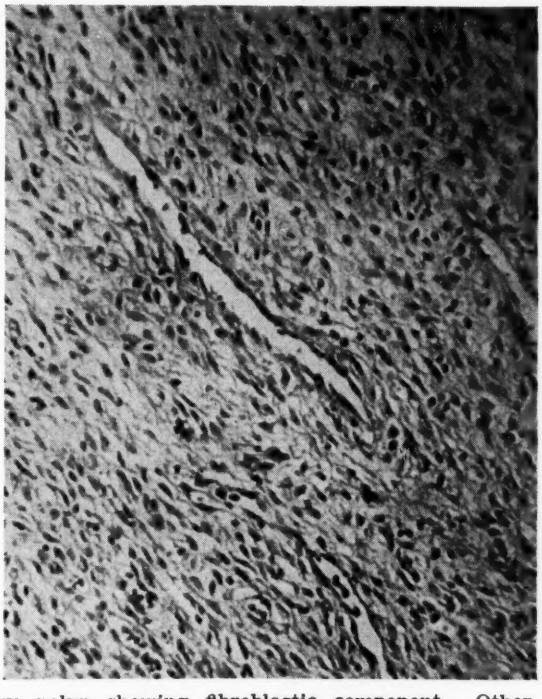


Fig. 11.—Inflammatory polyp showing fibroblastic component. Other sections show many inflammatory cells. (×300; reduced ¼.)

zone of severe inflammation, and, finally, in its deepest portion, of many capillaries separated by loosely arranged spindle-shaped cells. Bullock and Moran have reported a group of 5 cases of similar histology occurring in the stomachs of elderly individuals, and have labeled them "inflammatory fibroid polyps." We feel that our case is an example of an inflammatory condition in the uterus of an elderly woman who had prior radium insertion. Our revised diagnosis, in this instance, is "inflammatory fibroid polyp."

The 5 mixed mesenchymal sarcomas contained either cartilage, osteoid tissue, or areas simulating striated muscle. In the poorly differentiated areas, present in all cases, there was little question as to the malignant characteristics. In several areas of 2 cases atypical glands which might reasonably be interpreted as carcinomatous changes were present, but, actually, in terms of volume, comprised only a small part of the neoplasm. The presence of such areas led to a previous diagnosis of carcinosarcoma in these cases. In this regard it is our feeling that the term "carcinosarcoma" for tumors composed of adenocarcinomatous structures intermingled with areas of mixed mesenchymal sarcoma is better designated as complete type of mixed mesenchymal tumor. The uterus, it will be recalled, is completely mesodermal in origin and therefore the glandular structures also arise from mesoderm. The term should therefore include epithelial structures within a tumor composed of mesenchymal elements with varying degrees of metaplasia or heterotopia. Adherence to this principle will, we believe, lessen the confusion regarding the use of the term "carcinosarcoma."

If the term "carcinosarcoma" is used only for adenocarcinomas with a sarcomatous stroma and is not used for "mixed mesenchymal sarcomas" or for the coincidental occurrence of a carcinoma and a sarcoma which have collided, then our series comprises only one example of true "carcinosarcoma." In this instance the sarcomatous stroma did not appear to be of a high grade of malignancy, although the glandular component was highly malignant.

Adenocarcinoma and sarcoma apparently arising independently and colliding was the original diagnosis in 2 cases of this series. In one instance a polypoid mass of low-grade spindle-cell sarcoma of fibroblastic type formed an intracavitary growth, surrounded by adenocarcinoma invading the base of the sarcomatous polyp.

The second reported collision tumor consisted of a bulky necrotic intracavitary polyp composed of highly pleomorphic, large spindle-shaped cells which, in several areas, surrounded a normal but cystic endometrial gland. At the edges of the polyp, encroaching upon the endometrial surface of the uterus proper and infiltrating into the myometrium, were areas of adenocarcinoma.

In one case (Fig. 12) a diagnosis of leiomyosarcoma was made in 1942 upon the study of large amounts of curetted material. The tumor was rediagnosed as a rhabdomyosarcoma. Cross striations (Fig. 13) were definitely present and had apparently been overlooked. No other elements were found so that we do not feel justified in regarding this as a mixed mesenchymal sarcoma, although we are aware that the uterus was not excised in this patient.

Fig. 12.

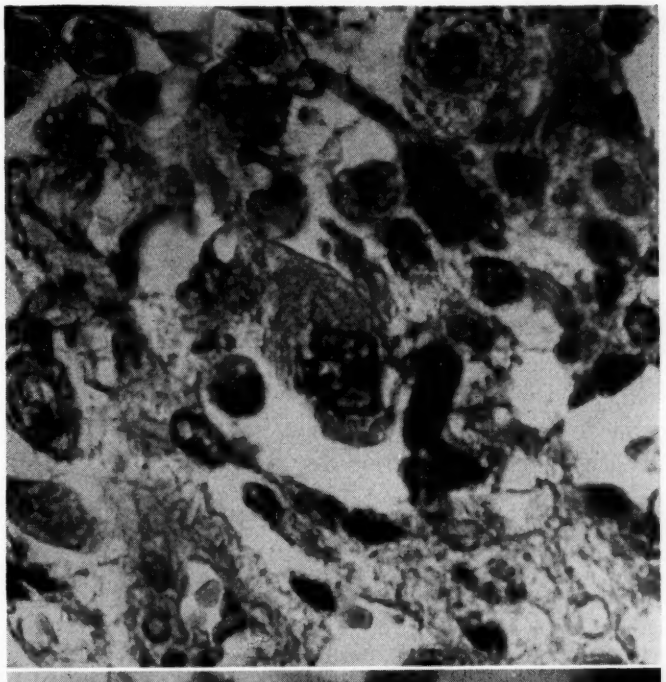


Fig. 13.

Fig. 12.—Rhabdomyosarcoma. (×600; reduced ¼.)

Fig. 13.—Rhabdomyosarcoma. This figure demonstrates cross striations. (×1,200; reduced ¼.)

Effect of Prior Radiation

Eight of the 49 patients studied had an artificial menopause induced by radiation. Radiation was administered for presumably benign uterine bleeding. Five of these patients subsequently developed malignancy, one within two years of radiation, and in 4 the sarcoma developed many years later. In the first case the malignancy may have been present at the time of the irradiation. In the latter group the radiation may possibly have served as a carcinogen. The intial cause of the bleeding might be the cancer precursor, however, rather than the irradiation. MacFarlane, in discussing this matter, refers to the possibility of the inherent susceptibility to malignancy in the patient who requires irradiation to cause a cessation of bleeding. Speert and Peightal reported malignancy of the uterus following radiation therapy. Lacassagne experimentally produced sarcoma in the thighs of rabbits by radiating the previously inflamed tissues; this same mechanism may function in the human endometrium.

Our cases with previous radiation are listed in Table III.

TABLE III. CASES PREVIOUSLY RADIATED FOR BENIGN LESIONS

NO.	DIAGNOSIS	TYPE RAD.	AGE	TIME INTERVAL	RESULT
Short Interval.—					
1.	Primary leiomyosarcoma	X-ray	50	1 year	Died post-operatively
2.	Stromatous endometriosis	Radium	68	3 years	Alive
3.	Cellular myoma	Radium	46	1½ years	Alive
4.	Cellular myoma	Radium	42	3 years	Alive
Long Interval.—					
5.	Mixed mesenchymal	Radium	54	6 years	Died
6.	Collision carcinosarcoma	Radium	42	21 years	Died post-operatively
7.	True carcinosarcoma	Radium	50	14 years	Died
8.	Primary leiomyosarcoma	X-ray	37	9 years	Died

Symptoms

The most common symptoms in patients with sarcoma were bleeding and abdominal mass. Vaginal bleeding was absent in only 5 cases. In 11 cases postmenopausal bleeding was the presenting symptom. Five patients presented with mass and abdominal enlargement. One patient, in addition to bleeding, complained of vertigo and diplopia, and was subsequently found to have cerebral metastases. No exfoliative cytological studies were done on any of these patients.

The incidence of postmenopausal bleeding in the endometrial and mixed mesenchymal groups was relatively high due to the fact that this type occurs in the older age group and also because of the direct involvement of the endometrium. Eight of the 11 endometrial sarcomas were postmenopausal. The type of bleeding associated with the nonendometrial sarcomas was more likely to be of the irregular menopausal or premenopausal type so often seen in the menstrual life of many patients.

The symptoms in order of frequency in this series were: postmenopausal bleeding, irregular bleeding during menstrual life, mass, pain, vaginal discharge, and weight loss.

As can be seen by the nonspecific pattern of the symptoms, the diagnosis was most frequently made in the laboratory.

One patient was admitted to the hospital in shock, and at operation was found to have a perforation of the uterus by the growth of a mural sarcoma with a diffuse spread through the pelvic viscera.

Sarcoma of the uterus was found in only one Negro woman, despite the high incidence of leiomyomas in this race. The sarcoma in this case was of the endometrial type. Bosse and Stanton report only two cases in Negroes in their 27 sarcomas. Recently, however, Williams reporting 15 sarcomas from Kentucky, found that 14 of his patients were Negroes.

The incidence of sarcoma arising in a fibroid varies with the series reported, the highest incidence being 10 per cent as reported by Warnekros and the lowest reported by Pfannenstiehl as zero per cent. Kimbrough reported 0.76 per cent, Finn 0.3 per cent, Randall 0.19 per cent, and Novak 0.52 per cent. Ewing thought that sarcoma arising in a myoma was rare.

There were three patients with a previous history of myomectomy, two operated upon nine years and one three years before the diagnosis of sarcoma was made. Two of the cases were diagnosed by us as leiomyosarcoma, one secondary in a previously existing myoma and one as a primary mural type. The third case was an unclassifiable tumor with malignant features. In this latter case a review of the old slides obtained at the time of the previous operation showed the same lesion present, and also in the operative note it was stated that the "fibroid" did not shell out of its capsule easily. This tumor was originally diagnosed as a leiomyoma.

Thirteen of the patients were postmenopausal, 8 with a natural menopause and 5 with an induced menopause. Eight of the postmenopausal patients had endometrial sarcoma, mixed mesenchymal sarcoma, or carcinosarcoma. Three had primary mural sarcoma, one secondary, and one unclassified sarcoma.

Seventeen of the patients were parous, 11 nulliparous, and two of unknown parity. Eleven of the parous group had endometrial sarcoma. The youngest patient was 27 years of age and the oldest was 65. The endometrial type was in the older age group as a rule.

The present treatment of uterine sarcoma is surgery and postoperative radiation. Many of our patients were treated by supracervical hysterectomy because their cases occurred prior to the widespread use of total hysterectomy and because of the unsuspected diagnosis. In the light of our present knowledge and techniques, it may seem advisable to do the more radical operation in the cases diagnosed before surgery and without evidence of distant metastases. In this series there were 6 total hysterectomies, 19 supracervical hysterectomies, one vaginal hysterectomy, in 2 instances only partial removal of an extensive mass was done, and one case was treated with radium alone; 9 patients received x-radiation postoperatively. Three patients received radium following the diagnosis of curetted material and prior to hysterectomy. The late diagnosis of this disease hinders the application of more definitive forms of treatment.

Table IV gives the treatment and results.

TABLE IV. TREATMENT AND RESULTS

	TREATMENT	RESULT	TIME
Endometrial.—			
1	Total hysterectomy	Alive	1 year
2	Total hysterectomy	Alive	6 years
Mixed Mesenchymal.—			
1	Supracervical hysterectomy and x-ray	Died	
2	Supracervical hysterectomy and x-ray	Died	
3	Supracervical hysterectomy and x-ray	Died	
4	Supracervical hysterectomy and x-ray	Alive with metastases	2 years
5	Total hysterectomy	Died	
Rhabdomyosarcoma.—			
1	Radium	Died	
Carcinosarcoma.—			
1	Total hysterectomy	Died postoperatively	
2	Supracervical hysterectomy	Alive	1½ years
3	Radium and supracervical hysterectomy	Died	
Primary Mural.—			
1	Supracervical hysterectomy	Died	
2	Supracervical hysterectomy	Died	
3	Total hysterectomy and radium	No follow-up	
4	Supracervical hysterectomy and x-ray	Died	
5	Supracervical hysterectomy and x-ray	Died postoperatively	
6	Supracervical hysterectomy	Alive	5 years
7	Supracervical hysterectomy	No follow-up	
8	Supracervical hysterectomy and x-ray	Died	
Secondary Sarcoma in Myoma.—			
1	Partial removal mass	Died	
2	Partial removal mass, radium and x-ray	Died	
3	Supracervical hysterectomy	Died	
4	Supracervical hysterectomy and x-ray	Died	
5	Supracervical hysterectomy	No follow-up	
6	Supracervical hysterectomy and x-ray	Alive	4 years
Unclassified.—			
1	Supracervical hysterectomy	Died	
2	Total hysterectomy	Alive	5 years
3	Vaginal hysterectomy	Alive	10 years
4	Supracervical hysterectomy	Alive	16 years

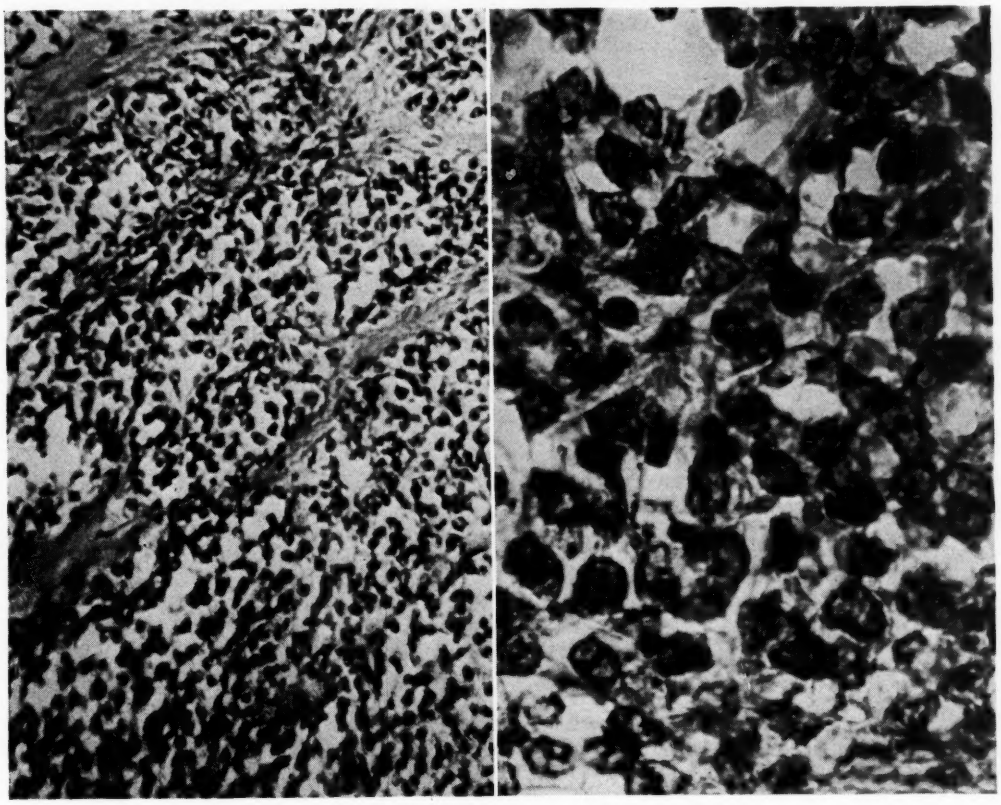
Comment and Results

Our findings are similar to those reported by other authors, except for the relatively low incidence of secondary sarcomas. This latter group and the primary mural group are the neoplasms eliciting contrary opinions when reviewed by several pathologists. The rigidity of the standards of malignancy frequently alters the end results considerably. There are two extremes as previously mentioned, the one holding that without evidence of metastases or death there is no real proof of malignancy, and the other calling any tumor with occasional mitotic figures or giant cells malignant. It is clear to see how the results can be affected by the pathologist's point of view. We attempted to establish malignancy by the criteria as discussed in the section on pathology.

Fenton reported a series with a 77 per cent survival rate in the sarcomas arising in leiomyomas. We realize that with such small series of cases any percentage figures can be very misleading, but it seems the discrepancy here is due

to differences in histological interpretation. When one considers the total survival rate of different authors, this again varies. Novak and Anderson reported a survival rate of 30 per cent, Randall 31 per cent, Williams 15 per cent, and Thornton and Carter 8 per cent.

Of our 29 patients with sarcoma of the uterus, 2 died postoperatively. Of the 27 remaining, 15 have died of the disease, 9 patients are alive, one with known metastases and 4 with less than five years' follow-up study. No follow-up data were obtainable for 3 patients. Four of the 5 patients with mixed mesenchymal sarcoma are dead and the remaining one has known metastases; of the 3 with carcinosarcomas, one is dead of the disease, one died of postoperative



A. *B*

Fig. 14.—*A*, Endometrial stromal sarcoma. This tumor was composed of endometrial stromalike cells and the diagnosis of malignancy is based upon myometrial invasion. (×300; reduced ¼.)

B, High-power view of Fig. 14, *A*. (×600; reduced ¼.)

complications, and one patient is alive one and one-half years after surgery. Of the primary mural sarcomas, 5 of the 8 patients are dead, in 2 cases there was no follow-up obtainable, and one patient is alive five years later. Of the unclassified tumors, one patient is dead and 3 are alive more than five years. This unclassified group gave us much trouble and possibly the last chapter has not been written on this group of unusual tumors. The secondary leiomyosarcoma group, in which there are 6 cases, shows 4 patients dead of the disease, one alive

and well four years later, and one case with no follow-up data obtainable. The 2 patients with endometrial sarcomas (Fig. 14, *A* and *B*) are alive and well, one more than five years and the other for two years.

Tables V and VI summarize our results.

TABLE V. FINAL RESULTS

TYPE	NO.	DEAD	ALIVE	DURATION	NO FOLLOW-UP	METASTASES
Endometrial	2	0	2	1 year 6 years		
Mixed mesenchymal	5	4	1	2 years		1
Rhabdomyosarcoma	1	1				
Carcinosarcoma	3	2	1	1 year		
Primary mural	8	5	1	5 years	2	
Secondary in myoma	6	4	1	4 years	1	
Unclassified	4	1	3	7 years 5 years 10 years		
	29	17	9	Less than 5 years 4	3	1

TABLE VI. SUMMARY OF END RESULTS

	NUMBER	PER CENT
1. Total cases	29	
2. Cases with unknown result	3	
3. Cases with known result	26	100
4. Died of sarcoma	15	57
5. Died of operative complications	2	8
6. Alive with metastases	1	4
7. Alive and well less than five years	3	11
8. Alive and well more than five years	5	19

If we accept the cases lost to follow-up as dead of the disease and eliminate the post-operative deaths and the patients alive less than five years, our corrected mortality rate then becomes 78 per cent.

Summary

Forty-nine cases originally diagnosed as sarcoma of the uterus were critically reviewed. Twenty-nine of the cases proved, upon review, to be sarcoma and 20 were not. Sixteen of the 20 cases ruled out of the sarcoma group were benign. Our criteria for the diagnosis of sarcoma have been stated. More sections from blocks and the cutting of additional blocks, as well as the use of special stains, can aid in the diagnosis. The knowledge of what is not sarcoma and familiarity with some of the less common tumors of the uterus can greatly facilitate the correct diagnosis of sarcoma.

There are no symptoms characteristic of sarcoma. The diagnosis is most often made in the laboratory. The treatment is surgical if no distant metastases are present.

In this series the prognosis was poor; 57 per cent of the patients have already died and only 5 patients, or 19 per cent, are alive more than five years. Our corrected mortality rate is 78 per cent.

Addendum.—Additional material from a private collection has been obtained since completion of this paper. One of the cases we diagnosed as anaplastic carcinoma is reclassified as mixed mesenchymal sarcoma.

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SARCOIDOSIS OF THE UTERUS

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SARCOIDOSIS is a generalized, chronic disease characterized by the presence of epithelioid-cell granulomas, particularly involving the lymph nodes, lungs, eyes and skin. Dissemination to other organs may occur, however. This communication is concerned with an unusual localization of sarcoidosis, namely, the uterus. It emphasizes the fact that on rare occasions evidence of sarcoidosis may be encountered in endometrial curettings or in extirpated uteri. In addition, it is observed that the histological appearance of the epithelioid-cell tubercles of sarcoidosis may readily be mistaken for the more commonly occurring tuberculous or foreign body granulomas.

Case Report

W. P., a 39-year-old married Negro woman, was admitted to the Gynecological Service of the Mount Sinai Hospital on Jan. 23, 1953. She complained of intermittent vaginal protrusion over a five-year period and of urinary stress incontinence of several months' duration. The obstetrical history included one incomplete abortion in 1946, one premature delivery in 1948, and five full-term normal spontaneous deliveries between 1934 and 1951. The menses had always been regular, occurring at 28-day intervals with a normal three-day menstrual flow.

The patient had lived in South Carolina until the age of 17 years, when she migrated to New York City. As a child she had been told she had asthma. During the past ten years occasional wheezing and a dry cough were noted.

Physical examination showed a well-developed woman in no acute distress. Auscultation of the chest disclosed the presence of occasional musical râles and coarse wheezing bilaterally. The heart sounds were of normal quality and there were no murmurs. The blood pressure was 140/85. The liver and spleen were not palpable.

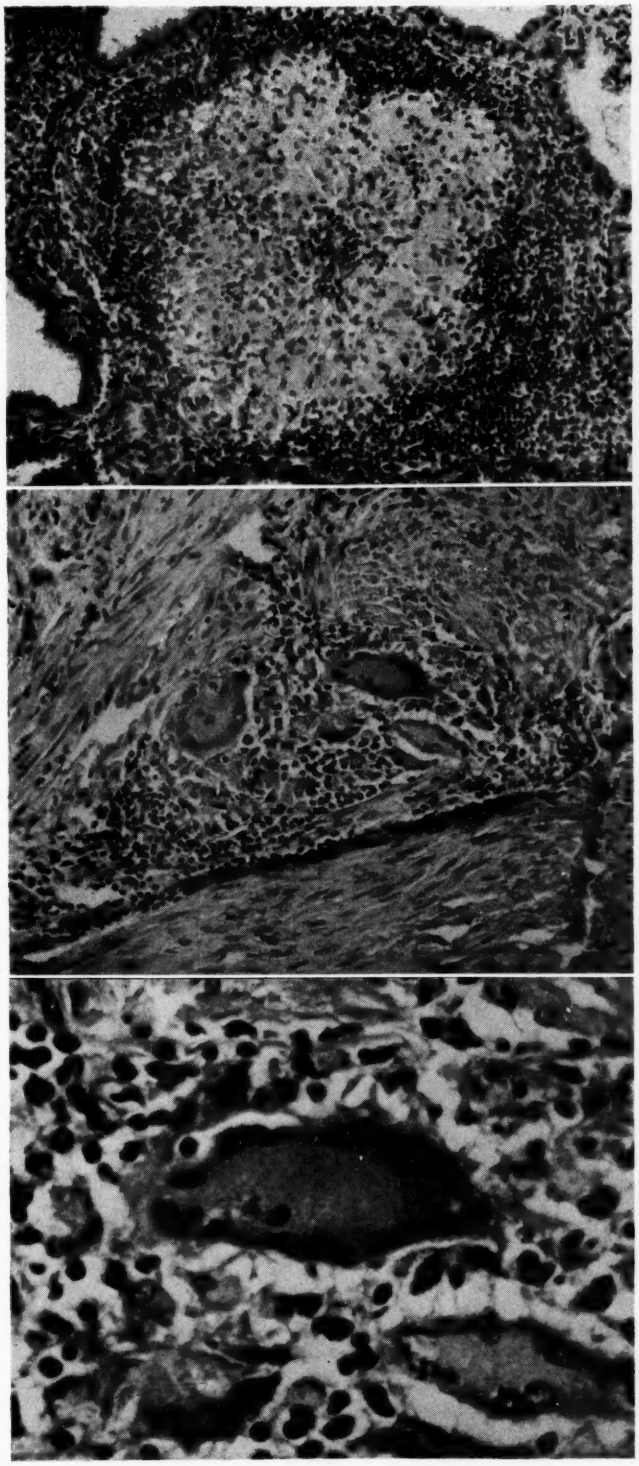
Pelvic examination disclosed a moderate cystourethrocele and a large rectocele. The cervix was lacerated and descended moderately on straining. The uterus was slightly enlarged by the presence of a fibromyoma. The adnexa were felt to be normal.

Laboratory Findings.—Laboratory studies showed a normal white blood count, erythrocyte sedimentation rate, blood urea nitrogen, and fasting blood sugar. The electrocardiogram, the venous pressure, and a chest roentgenogram were also normal.

In view of the patient's age, multiparity, and the presence of a fibromyoma it was considered advisable to remove the uterus at the time of the vaginal plastic repair.

Surgical Procedure.—Under spinal anesthesia a vaginal hysterectomy, urethroplasty, and anterior and posterior colporrhaphy were performed. The adnexa appeared grossly normal and accordingly were not removed. The patient withstood the surgical procedure well.

Pathological Examination.—The specimen consisted of a slightly enlarged uterus measuring 11 by 6 by 3.5 cm. Section through a subserous nodule in the fundus showed the typical, whorllike appearance of a fibromyoma. Within the myometrium several minute pinkish areas were noted. The endometrium appeared moderately thickened and succulent. *Microscopic examination:* The endometrium was found to be in a secretory phase. Conspicuous granulom-



A.

B.

C.

Fig. 1.—*A*, Granuloma of sarcoidosis within the endometrium. The noncaseating tubercle is composed of large, pale-staining, polygonal, epithelioid cells with peripheral lymphocytic infiltration. Note absence of necrosis, hyalinization, or fibrosis. (×200; reduced ⅓.)

B, Sarcoid tubercle within uterine myometrium composed of epithelioid cells, lymphocytes, and giant cells. Acid-fast bacilli could not be demonstrated. (×250; reduced ⅓.)

C, High-power view of giant cells in sarcoid tubercle of myometrium showing presence of asteroids. (×425; reduced ⅓.)

Fig. 2. Fig. 3. Fig. 4.

Fig. 2.—Chest roentgenogram (Nov. 5, 1948). Sarcoidosis manifested by bilateral hilar lymph node enlargement, more marked on the right. A dense infiltration extends into the right lung field at the level of the second and third interspaces anteriorly.

Fig. 3.—Chest roentgenogram (Jan. 21, 1952) showing marked regression of the lymph node enlargement in the right hilar region. The right pulmonary infiltrations have disappeared. The nodes at the left lung root are still prominent and new strandlike infiltrations extend upward and outward into the first and second interspaces anteriorly.

Fig. 4.—Chest roentgenogram (Jan. 29, 1953) showing both hilar regions and lung fields to be within normal limits. The changes observed in this series of roentgenograms (Figs. 2, 3, and 4) are considered characteristic of a regressing sarcoidosis.

atous lesions were scattered throughout the endometrium and myometrium. The granulomas consisted of epithelioid-cell tubercles without caseation (Fig. 1, *A*). Occasional giant cells were present (Fig. 1, *B*). A few of these contained asteroids and other inclusion bodies (Fig. 1, *C*). Tissue stains for acid-fast bacilli disclosed no organisms. The microscopic appearance was considered compatible with a diagnosis of uterine sarcoidosis.

In view of the histological findings, the patient was more closely questioned regarding her previous history. It was discovered that she had been attending the Chest Clinic irregularly during the previous five years. Her presenting symptoms there had been chronic intermittent cough and wheezing of ten years' duration. A chest roentgenogram made on her clinic admission in 1948 showed the following: There was considerable enlargement of the lymph nodes in both hilar regions. These were more prominent on the right where dense infiltrations extended into the lung fields at the level of the second and third interspaces anteriorly (Fig. 2). Mantoux tests carried to 1:100 dilution of old tuberculin were negative. Repeated search for acid-fast bacilli in the sputum disclosed no organisms. These findings supported the clinical impression that the patient had sarcoidosis. At that time no other localization of the disease could be detected. Slit-lamp examination of the eyes on two occasions failed to reveal any evidence of uveitis. The hemogram, sedimentation rate and urine analysis were normal, and the blood Wassermann test, negative.

The patient did not appear again at the Chest Clinic until January, 1952. She reported that she had had a normal full-term delivery in September, 1951. A chest film at this time, four years after the initial roentgenogram, disclosed almost total regression of the lymph node enlargement at the right lung root. The previously described pulmonary infiltrations had also disappeared. However, the nodes at the left lung root were still prominent, and strand-like infiltrations extended into the first and second interspaces (Fig. 3). One year later, at the time of vaginal surgery, the chest film showed no obvious abnormalities (Fig. 4). The changes observed in this series of roentgenograms were considered characteristic of a regressing sarcoidosis.

Postoperatively, further investigations were made relating to the sarcoidosis. The serum proteins were within normal limits; total protein, 6.7 Gm. per cent, with albumin 3.9 Gm., and globulin 2.8 Gm. per cent. X-rays of the bones of the hands and feet showed no cystlike changes. Tuberculin tests were repeated, utilizing purified protein derivative in first and second strengths, and were still negative. A Nickerson-Kveim cutaneous reaction for sarcoidosis was also negative at this time. There were no cutaneous lesions or palpable peripheral lymph nodes for biopsy. The patient refused scalene-fat-pad exploration as well as liver puncture.

Comment

Sarcoidosis is a disease of unknown etiology. Though any organ may be affected there is a predilection for the involvement of lymph nodes, lungs, eyes, skin, liver, spleen, salivary glands, and bones of the hands and feet. The disease may be disabling but is more often relatively benign. The typical lesion of sarcoidosis is a tubercle composed of a focal accumulation of large, pale-staining epithelioid cells, with occasional giant cells and lymphocytes. There is no evidence of caseation, but fibrinoid changes in the central portion of the tubercle are sometimes present. The granulomas appear intermittently in crops, remain stationary for a time, and then heal by hyalinization and fibrosis. It is not uncommon for regression to occur at one site while new foci of involvement are making their appearance.

Young adults are most often affected, Negros more often than white persons. Symptoms may be few or absent. Suggestive features include malaise, low-grade fever, cough, visual disturbances, hepatosplenomegaly, lymph node enlargement, and cutaneous lesions occurring particularly about the mucocutaneous junctions of the mouth and nose. Chest roentgenograms may show changes in

the pulmonary fields as well as bilateral hilar lymph node enlargement. Laboratory studies may give evidence of a hyperglobulinemia, increased serum calcium, an increased erythrocyte sedimentation rate, and occasionally a mild eosinophilia. The Nickerson-Kveim intracutaneous test made with a sarcoid tissue suspension has been found to be positive in 86 per cent of biopsy-confirmed cases.[1] This test may give a negative result during remission of the disease. Prognosis, though usually good, must be guarded. Blindness, pulmonary insufficiency, "cor pulmonale," or a superimposed tuberculosis may occur. Cortisone and corticotropin may offer relief for patients with active and severe disease processes. Hormonal therapy appears to be more effective in fresh cases than in older ones.[2, 3, 4]

Reported instances of sarcoidosis of the female genitals are rare. In 1933, Garland and Thompson[5] described a case of uveoparotid fever of Heerfordt in a 28-year-old woman with generalized dissemination of miliary nodules. There were no gynecological symptoms except for two episodes of amenorrhea lasting five months and two months, respectively. A von Pirquet test had been negative. At postmortem examination, noncaseating tubercles were found in the lungs, heart, liver, kidneys, lymph nodes, salivary glands, peritoneum, as well as in the endometrium, myometrium, and serosa of the uterus. Acid-fast bacilli could not be demonstrated by guinea pig inoculation of sputum, nor could they be identified in the tissues. Although Garland and Thompson believed this case to be one of atypical tuberculosis, it is now considered a classical instance of generalized sarcoidosis.

In 1941, Longcope[6] mentioned a case in which sarcoid epithelioid bodies were found in endometrial curettings. This is the only previous instance of uterine involvement that we could find in the American literature. Longcope's patient was a 29-year-old Negro woman with menorrhagia who had sarcoidosis of the mediastinal, cervical, and submaxillary lymph nodes. No mention was made of a node biopsy report. She remained well while under observation for fifteen years, with gradual disappearance of the mediastinal shadows.

Engelhard[7] in 1946 described two cases of uterine sarcoidosis. A 64-year-old woman with enlarged hilar nodes, bone involvement, and weakly positive Pirquet test was investigated for postmenopausal bleeding. The findings on pelvic examination were normal. Scanty curettings were obtained which revealed scattered lightly stained areas containing giant cells. These were considered to be sarcoid bodies. The second case was that of a primigravida with diffuse bilateral pulmonary lesions and a negative tuberculin test. The patient complained of metrorrhagia of four months' duration. The uterus and adnexa were found to be normal on physical examination. Biopsy of the cervix and curettings of the uterus disclosed lesions which the author considered to be compatible with sarcoidosis. There were scattered giant cells and no caseation. The cervical biopsy site healed uneventfully and the metrorrhagia did not recur. In neither of Engelhard's cases was lymph node or other tissue biopsy confirmation of the diagnosis obtained.

Naumann[8] in 1938 reported a case of diffuse miliary granulomatosis in a 4-month-old female infant. The tuberculin test had been negative to 10 mg. of old tuberculin. At necropsy there was involvement of liver, spleen, meninges,

choroid of the eyes, kidneys, skin, stomach wall, and periportal lymph nodes. There were also some subserous nodules in the genital tract. A detailed microscopic description was omitted by the author but he viewed his case as one of "diffuse sarcoid atypical lymphogranulomatosis." Thus, in three of the cases reported in the literature (Longcope, one case; Engelhard, two cases), the finding of sarcoid bodies in the uterus was apparently the only biopsy evidence of disseminated sarcoidosis elsewhere in the body.

Clinically, of the six cases of possible uterine sarcoidosis, including our own, one manifested menorrhagia, another metrorrhagia, and a third, postmenopausal bleeding. In these it is highly questionable whether the symptoms had any relationship to the involvement of the uterus with sarcoidosis. It is apparent, as our case illustrates, that uterine sarcoidosis, like pulmonary and hepatic sarcoidosis, may be symptomless. In view of the generalized nature of this disease, it is possible that careful pathological examination after pelvic surgery may reveal a higher incidence of uterine involvement.

The history of our patient indicates that she had been gravid seven times, with five normal, full-term pregnancies. The last pregnancy had occurred in 1951 when the pulmonary sarcoidosis was still active, although regressing. The patient apparently had no difficulty in becoming gravid, nor was the pregnancy adversely affected. This conforms with the experience of the Mount Sinai Hospital Sarcoidosis Clinic as well as with reports by other groups. In short, sarcoidosis per se does not influence fertility, pregnancy, labor, or the health of the newborn infant. If vital organs are not formidably impaired, sarcoidosis should not be considered a contraindication to pregnancy. Conversely, pregnancy does not appear to influence the course of sarcoidosis significantly.

It is of interest to note that sarcoidosis may also involve the breast, although infrequently. The lesion may be manifested by nontender, firm, movable nodules or masses which on biopsy or excision revealed characteristic sarcoid granulomas. Sometimes a nodule apparently lying within the periphery of the breast may on biopsy be revealed as a lymph node with sarcoid involvement. Spontaneous regression may occur. Lofgren[9] has noted that among his female patients with sarcoidosis a high proportion had had their first clinical manifestations of the disease during pregnancy and lactation.

In our patient, a comparison of roentgenograms of the chest taken in 1948 and 1953 (Figs. 2, 4) indicated a marked regression of the hilar lymph nodes and pulmonary lesions. Histologically, such healing is manifested by fibrosis, hyalinization, and possibly resorption of the granulomas. However, the sarcoid tubercles in the extirpated uterus (Fig. 1, *A*, *B*, and *C*) appeared florid, with no evidence of hyalinization or fibrosis. This disparity between the chest and uterine findings is common, since crops of tubercles in different parts of the body may appear, remain stationary for years, and progress or retrogress independently.

In a known case of sarcoidosis, the finding of epithelioid-cell granulomas in the uterus should present little diagnostic difficulty. In the absence of clinically obvious sarcoidosis, however, the differential diagnosis of uterine granulomas may be difficult. Histologically, the lesion of a sarcoidosis is a discrete granuloma composed of epithelioid cells, with occasional giant cells and few lympho-

cytes. In contrast to tuberculosis, there is no caseation necrosis, liquefaction, or gross calcification. Acid-fast bacilli cannot be demonstrated by stain or guinea pig inoculation. Schaumann bodies, though nonspecific, may at times be found in the giant cells. They are apparently not present in tuberculosis.[11] Regression of the sarcoid granuloma is often accompanied by the deposition of eosin-staining para-amyloid material at the periphery of the sarcoid body, the process progressing centripetally. Like tuberculosis, sarcoidosis may involve the cervix, endometrium, or myometrium. In contrast to pelvic tuberculosis, however, tubal involvement has not been reported.

Though an isolated lesion may present the histological features of sarcoidosis, the diagnosis must be further substantiated by multiorgan involvement. Confirmatory biopsy of an enlarged lymph node or skin lesion, typical roentgen changes in the lungs and mediastinal nodes, hepatosplenomegaly, and involvement of the eyes or salivary glands are to be sought. As stated, the Nickerson-Kveim test is frequently positive and the tuberculin test is usually negative. Hyperglobulinemia and hypercalcemia may occur.

The characteristic lesion of tuberculosis of the uterus is an epithelioid-cell granuloma which may contain giant cells, polymorphonuclear leukocytic infiltration in and around the tubercle, and central necrosis and caseation. Healing is evident in fibrous encapsulation and scarring. Schaumann bodies are lacking, but stellate inclusions in the giant cells may be found rarely.[12] Acid-fast bacilli may be demonstrated by tissue stains, by culture, or by guinea pig inoculation with tissue, uterine secretion, or menstrual blood. In spite of all these differences between the granuloma of sarcoidosis and tuberculosis, it may be impossible to distinguish between them histologically. Clinically, pelvic tuberculosis is usually symptomatic. The history may include menstrual aberrations, amenorrhea, sterility, and a previously known pulmonary tuberculosis. A tuberculous salpingitis is almost invariably present. The tuberculin test is positive.

Foreign body granulomas are nonspecific. Histiocytes and giant cells prevail. The latter may occasionally contain stellate inclusions.[12] If the foreign body is particulate, it may be evident within phagocytic cells. In the acute stages a polymorphonuclear infiltration may be seen, later replaced by round cells and evidences of fibrosis. A history of uterine infection, manipulation, surgical interference, or insertion of foreign bodies, particularly if followed by leukorrhea, is most suggestive.

Other diseases that may give rise to generalized granulomas include leprosy, coccidioidomycosis, and lymphogranuloma inguinale, but involvement of the uterus by these diseases is very infrequent. Leprosy of the uterus has not been encountered at the Carville Leprosarium.[13] A report from the Japanese literature,[14] however, indicates that on rare occasions the uterus may be affected. According to this report, lesions containing acid-fast lepra bacilli were encountered in the myometrium, and lepra cells were found in the endometrium, Fallopian tubes, and the vagina. The ovaries are almost never involved, in contrast to the testes which are commonly affected in lepromatous leprosy. Sterility in women is unusual.

We could find no reference to histoplasmosis of the female genital tract, although involvement of the male urogenital tract has been described.[15, 16, 17]

Skin tests with histoplasmin, complement-fixation tests, and special tissue stains for the fungus help differentiate this condition from sarcoidosis.

A diagnostically similar problem occurs in coccidioidomycosis where placental lesions as well as adnexal involvement, unassociated with uterine lesions, have been described.[18, 19] A history of exposure in endemic areas, the finding of typical endospores of *Coccidioides immitis*, and a positive coccidioidin intradermal test help establish this diagnosis.

Epithelioid-cell granulomas have been described in the cervix in granuloma inguinale. The finding of Donovan bodies, as well as the clinical course, helps to clarify the etiology.[20]

In the early phase of ulceration, lymphogranuloma inguinale (lymphopathia venereum) may exhibit pseudotubercles with macrophages and giant cells in the cervix.[21] The diagnosis is aided by the absence of caseation, the development of regional adenitis, the clinical course, and a positive Frei test.

Summary

1. A case of generalized sarcoidosis with asymptomatic uterine involvement is reported. Characteristic epithelioid granulomas were found in the endometrium and myometrium of a uterus removed by vaginal hysterectomy.

2. Although sarcoidosis is a systemic affection with multiorgan involvement, localization in the uterus is extremely rare. A survey of the literature discloses reports of only five previous instances of uterine sarcoidosis.

3. Though in three cases curettage was performed for abnormal bleeding, it seems unlikely that the sarcoid uterine granulomas were responsible for the symptoms.

4. The finding of tuberclelike granulomas in the endometrium or myometrium should alert one to the possibility of sarcoidosis. The diagnostic criteria of this disease are described. Differentiation must be made from tuberculous and foreign body reactions.

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ENDOMETRIAL CARCINOMA

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THE literature continues to be filled with an abundance of material concerning both carcinoma of the cervix and carcinoma of the endometrium. The very destructive nature of these conditions and the great necessity for improvement of their cure justify all that can be added to the written volumes, as long as progress continues. A review of modern literature shows how necessary it is for institutions with a large patient census repeatedly to take inventory of their experiences and compare them with those already reported. This is especially so when in a widely reported and distributed article the incidence of carcinoma of the endometrium to carcinoma of the cervix continues to be quoted as 1 to 10. Is this a true picture of the incidence? What has been our experience? To evaluate this experience with carcinoma of the endometrium in a part of the Milwaukee area, such an inventory was made in two of the large teaching institutions during the ten-year period from 1942 to 1952. During this period 9,560 gynecological patients, practically all of whom were private patients, were admitted to Milwaukee Hospital, while 6,531 gynecological patients, all indigent, were admitted to the Milwaukee County Hospital.

Incidence and Economic Status

It has always been our impression that the end results of the treatment of uterine carcinoma depended to a considerable extent upon the economic status of the women involved. We are of the opinion that patients in the lower income group often fail to seek medical care during the early stages of the disease. This has been substantiated by the fact that during this ten-year period only 8 patients at the county hospital survived a five-year period after undergoing one of the accepted methods of therapy for endometrial carcinoma.

That the economic status along with the intellectual capacity of the indigent patient may play a part in her chances of developing a uterine malignancy is evident when one compares the incidence of cervical versus endometrial carcinoma as found in the two institutions. During this ten-year period the ratio of cervical to endometrial cancer at the County Hospital was 3.3 to 1 (seventeen authors quote 3:1 to 8:1; one authority mentioned in the opening paragraph quotes 10 to 1), while in our private patients we found a ratio of 1:1 which during the latter five years has changed to 4:5. What is the explanation? Can this be the result of a combination of better obstetrical care, early and adequate restoration of the cervix to a healthy state (cautery, conization of the cervix, and an attempt to restore the normal flora of the

vagina)? Can the answer be found in the yearly routine physical examination more frequently requested by the private patients and encouraged by all gynecologists who practice according to modern concepts? Will a still greater number of cases be revealed by routine office screening and biopsy methods if adopted in endometrial investigation as in cervical appraisal? The answer to this will be found when large series of cases are evaluated. Can the discrepancies in the ratios, as reported, be found in the very evident fact that there is certainly a great difference in the types of institutions that are reporting statistics? In the large teaching institutions with predominant charity services, the ratio may be very similar to that of the county hospital, 3.3 to 1. In large centrally located university centers, it is evident that the dreaded cancer of the cervix is sent to these centers for the complete irradiation therapy or the irradiation and radical surgical therapy that is now in vogue. It is understandable, however, that the erroneously less dreaded and wrongly minimized carcinoma of the endometrium is, in the early stages, more frequently cared for at the local level and then sent to the large centers, hence the 10:1 or 8:1 ratios. The truly large private hospital equipped for all types of therapy and staffed by gynecologists capable of administering all types of therapy is a photographic image of practice as seen in the representative gynecologist's office. Is the proportion 4 to 5 or 1 to 1 as seen at Milwaukee Hospital the true picture of this much discussed ratio?

Still another finding suggestive that the economic state of the patient plays a part in this picture is the fact that the average age of those entering the private hospital was 56 years while the age of those admitted to the county institution was 65.4 years. The highest average mentioned in the study made by 17 authorities was 59.9 years. That this is a disease of the later years of a woman's life is proved when one realizes that over 85 per cent of the entire group were 50 years of age or over.

The average parity for the two groups was Milwaukee Hospital 1.7 and Milwaukee County Hospital 2.8. This is probably of no significance other than to prove again that the lower income group have more babies. It is thought, however, that multiparity plays a part in the cervical cancer problem and the same may be true in endometrial cancer.

It is interesting to note that 96.4 per cent of the private patients reported abnormal bleeding and that on an average symptoms and signs had been present for from ten to eleven months. Will this be reduced when and if the value of routine endometrial screening is established?

Is the fact that 3.6 per cent of these patients have or have had multiple carcinomas of any significance? Since these patients are advanced in years may it not be due to prevalence of cancer during this period of life or is cancer a systemic disease?

Treatment

Numerous operators utilized various methods or combinations of the same for the treatment of endometrial carcinoma. There was no set plan adopted. Each physician chose whatever he considered the most adequate treatment for the individual patient. In the private series, very rarely was there any type of palliation used because of the physical condition of the patient. There were no lymphadenectomies performed and there were no operative deaths.

All of the operations performed were total hysterectomies with bilateral salpingo-oophorectomies with the exception of 14 subtotal and 4 vaginal extirpations. There were 60 private patients operated upon. Some had preoperative supervoltage roentgen therapy or intracavitary radiation or both. Others were subjected to postoperative supervoltage roentgen therapy and occasion-

ally radiation applied to the cervical stump following subtotal hysterectomy, while 70 per cent of the patients were subjected to panhysterectomies. The supervoltage radiation varied between 2,000 to 3,000 r delivered through four ports, two anterior and two posterior. The dose depended upon the amount of tissue traversed by the roentgen rays, skin tolerance, and the patient's ability to tolerate therapy. The intracavitary radiation was usually accomplished with a single intrauterine capsule although occasionally multiple applicators were used. The dosage varied from 2,400 to 6,000 mg. hr.

Results

The end results of these varied and multiple methods for the treatment of endometrial carcinoma, depending upon the extent of involvement of the uterus, have been studied depending upon whether the lesion involved only (1) endometrium, (2) extension into the myometrium, or (3) whether the lesion had advanced into the serosa, adjacent organs, or the lymph glands. These findings were based upon gross appearance, and the microscopic study of the excised tissue, together with the clinical findings at the time of operation.

The largest number of patients treated and successfully followed were those private patients treated at Milwaukee Hospital from 1942 to 1952. Table I demonstrates the fact that the survival rate depends more upon the extent of the lesion than it does upon the method of treatment.

TABLE I. THE FIVE-YEAR END RESULTS AT MILWAUKEE HOSPITAL OF VARIOUS TYPES OF TREATMENT BUT NOT INCLUDING RADIUM ALONE, X-RAY ALONE, OR RADIUM AND X-RAY

	OPERATION	OPERATION AND X-RAY	OPERATION AND RADIUM	OPERATION, X-RAY, AND RADIUM	TOTAL	TOTAL TREATED	RELATIVE CURE RATE
Endometrium Only.—							
Living	12	11	1	3	27	29	93.1%
Dead	0	2	0	0	2		
Endometrium and Myometrium.—							
Living	7	7	2	3	19	26	73.0%
Dead	3	4	0	0	7		
Beyond Myometrium.—							
Living	2	1	0	1	4	5	80.0%
Dead	0	0	1	0	1		
Total	24	25	4	7	50 10	60	83.3%

The highest relative cure rate was obtained where the carcinoma was found to be limited to the endometrium. Whether surgery alone or in combination with roentgen and radium therapy or either one or the other alone was used made very little difference in the over-all end results. The 29 patients of this group followed for five years or longer showed a relative cure rate of 93.1 per cent. It is interesting that the operation performed upon 15 of these patients was a subtotal hysterectomy followed by roentgen or radium therapy with a five-year survival rate of 82 per cent. Although subtotal or vaginal hysterectomy is not advocated as the operation of choice for endometrial carcinoma, nevertheless, it is interesting to note that this procedure was carried out in 33⅓ per cent. There were 4 vaginal hysterectomies with one death. Where the myometrium was involved the survival rate for those patients followed five years or more decreased to 73 per cent. Where the lesion extended beyond the uterus there were so few patients treated or operated upon that it was considered inadvisable to try to evaluate the end results. The over-all cure rate was 83.3 per cent.

An analysis of the end results obtained from all types of treatment of all the patients from both hospitals shows that the most satisfactory results were those in the private series where those patients who could not be followed plus the ones who died were all considered dead with a resultant absolute cure rate of almost 70 per cent. Contrast this with the very low rate of 47 per cent in the county hospital group. These results are shown in Table II.

TABLE II. THE FIVE-YEAR END RESULTS AT MILWAUKEE HOSPITAL AND MILWAUKEE COUNTY HOSPITAL

SERIES	NUMBER CASES SEEN	NUMBER CASES TREATED	DIED OF CA	DIED OF OTHER DISEASE	LOST	FIVE-YEAR CURE	CURE RATE %	
							ABSOLUTE	RELATIVE
Private	80	78	13	4	7	54	69.2	80.6
Ward	31	17	3	4	2	8	47	73
Total	111	95	16	8	9	62	65	80

A review of the literature detailing the methods of treatment and results obtained shows a great variation with no particular or singular method of therapy showing any great advantage over any other. The authors reported results compare very favorably with those listed in Table III.

TABLE III. END RESULTS OF THE TREATMENT OF ENDOMETRIAL CARCINOMA REPORTED BY OTHER AUTHORS IN CURRENT LITERATURE

TYPE OF TREATMENT	AUTHOR	RELATIVE FIVE-YEAR CURE %
Radium, x-ray and operation	Schmitz	65
	McLennon	90
	Randall	50
	Arneson	71
X-ray and operation	Miller	77
	Schmitz	60
	Randall	55
Radium and operation	Corscaden, et al.	70-90
	Stearns	86
	Randall	82
	Cosbie	84.6
Operation alone	Bastiaanse (Vaginal hysterectomies only)	72
	Randall	60
	Masson	66
	Dearnley (England)	78
	McKelvey (absolute rate)	81

It is our opinion that with the lesion limited to the endometrium any one of the accepted procedures mentioned will afford a five-year survival rate of from 80 to 90 per cent. If the lesion involves the myometrium a combination of supervoltage roentgen therapy and intracavitary radium followed at the appropriate time by total hysterectomy and bilateral salpingo-oophorectomy will end in a salvage rate of 60 to 70 per cent.

When the carcinoma has extended beyond the confines of the uterus the salvage rate is very much lower. Might it not be much wiser to direct the postoperative supervoltage roentgen therapy to the areas along the common iliac arteries and the aorta to destroy if possible metastases that are limited to these fields.

Causes of Death

Fifteen patients who died with a proved diagnosis of endometrial carcinoma following necropsy were considered to have died from uremia in 2 instances, gastrointestinal complications in 3, pulmonary metastases in 2, peritonitis in one, and from diseases unrelated to the uterine lesion in 7 others, 46.6 per cent, or almost one-half of the cases (Table IV).

TABLE IV. NECROPSY FINDINGS, MILWAUKEE COUNTY HOSPITAL

CAUSE OF DEATH	NUMBER OF CASES	%
Uremia	2	13.3
Gastrointestinal complication	3	20
Pulmonary metastases	2	13.3
Peritonitis	1	6.6
Unrelated disease	7	46.6
Total	15	

Seven of the 8 patients autopsied who died as the result of cancer were found to have distant metastases. The one without these metastases had an inadequately treated case and died of carcinomatous spill secondary to a spontaneous perforation of the uterus.

In addition, 2 patients who died of unrelated causes had distant metastases. If we delete the inadequately treated case, it appears that 9 of 9, or 100 per cent of treated patients with carcinoma of the endometrium will have distant metastases at death. Only 54.6 per cent of those in a similar study done on carcinoma of the cervix had distant metastases.

The sites of metastases are enumerated as follows:

Liver, Lung, Peritoneum	42%	Omentum, Bladder	22%	Primary node	9%
				Secondary node	33%
Ovary	33%	Kidney, Adrenal, Bowel, Abdominal wall	11%	Distant node	22%

In 7 autopsied patients the cause of death was found to be other than cancer. No carcinoma was found at autopsy in 2 of the patients. Three patients had resectable carcinoma in the pelvis which did not contribute to the death. The remaining 2 had metastases and would eventually have died of the carcinoma. These metastases were pulmonary in one and hepatic in the other case. As the result of the autopsy study, the following conclusions are evident:

1. Almost one-half of the patients died of other causes. Therefore, do not "doom" a patient to death because she is known to have cancer but rather look for "other" disease.
2. Local disease is rarely the cause of death in carcinoma of the endometrium.

Comments and Conclusions

The re-examination of the material presented indicated the fact that about 0.015 per cent of the patients admitted to the gynecological services of both the private and the charity hospital will have endometrial carcinoma.

A careful appraisal of reported statistics makes one look for the true ratio between endometrial and cervical carcinoma. Is it closer to 1:1 than to the accepted and frequently reported 8:1, 3.3:1, or 10:1?

The improvement in the detection of cervical cancer by popular accepted screening methods may indicate that similar methods adopted in endometrial carcinoma will result in earlier detection and increased cure. Our figures seem to indicate that early diagnosis and therapy started while the disease is limited to the endometrium will have more influence upon the cure rate than the specific type of therapy used.

When death is due to carcinoma, there are always distant metastases. This differs from carcinoma of the cervix, where there were distant metastases in only 54.6 per cent of the patients who died.

It is of great interest to note that one-half of the patients autopsied died of causes other than carcinoma. It is therefore essential that the cause of the current illness in a patient suffering from cancer not be interpreted as being directly due to the cancer alone. An accurate diagnosis of coincidental disease must be made in this as in any other patient.

Finally, the ultimate defeat of endometrial carcinoma, as of all carcinomas, is first by eternal vigilance, then by early diagnosis, and finally by the treatment indicated.

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MALIGNANT TUMORS OF THE OVARY

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DURING the past two decades the survival rate for ovarian carcinoma has remained essentially unchanged. This will no doubt remain true as long as we see the majority of patients for the first time in the more advanced stages of the disease. Because of their insidious onset and rapid spread through the abdominal cavity by implantation, tumors of the ovary give few alarming symptoms early. When first diagnosed, the majority of patients have extensive intra-abdominal metastases which cannot be completely removed by surgical means. No reliable laboratory tests or diagnostic procedures are available which might help to make an early diagnosis. The responsibility, therefore, lies with the physician and the patient. The physician should make frequent and accurate pelvic examinations and should educate the patient as to the early symptoms and signs found in this condition. This is especially true in those patients past the menopause. The patient's responsibility is to seek medical advice immediately when any such symptoms or signs develop. Carcinoma of the ovary is not a common disease, comprising only 4 per cent of all malignant tumors in women. Of all ovarian tumors, 15 per cent are malignant, and of these approximately one-half are bilateral.[20]

Material

The review of this material was undertaken in order to determine the advantage, if any, in the use of postoperative irradiation in various stages of carcinoma of the ovary. Between the years 1936 and 1949 a total of 100 cases of malignant ovarian tumors were seen at the White Memorial Hospital. Of these, 4 patients disappeared to follow-up immediately following operation and have not been seen since. They are, therefore, omitted from this study. The remaining 96 patients have all had adequate follow-up and will constitute the basis of this report.

Age Incidence.—The most common age was between 50 and 59 years (Table I). Thirty-three per cent of our patients were in this group. This agrees with the reports of other investigators who feel that most ovarian malignancies occur after the menopause.[10, 16, 19, 24] The youngest patient was 24 years and the oldest 82 years of age.

Marital Status.—Of the 78 married patients in this series, 18, or 23 per cent, had never been pregnant. This figure is high compared with the normal sterility rate in women which is commonly considered to be about 10 per cent.[18] In a recent series reported by Freed and Pendergrass,[6] they found that 42 per cent of the married women had never been pregnant. In this connection they discussed the possibility of a congenital developmental anomaly increasing the chance for the formation of a new growth.

TABLE I. AGE GROUPS

	NO. OF PATIENTS
Under 19	0
20-29	3
30-39	10
40-49	19
50-59	32
60-69	25
70-79	4
Over 80	3
Total	96

Race.—Eighty-two of the 96 patients were Caucasian, 13 were Negro, and in one case the racial status could not be determined.

Signs and Symptoms.—Gradual swelling of the abdomen commonly accompanied by pain is the most common, and often the only symptom. Complaints referable to the gastrointestinal and genitourinary tracts were also common and in most cases were apparently due to pressure from extrinsic masses or fluid. Other symptoms are listed according to their frequency in Table II. The incidence noted here agrees quite closely with that in other reported series. These symptoms are, in general, nonspecific, and in many cases are either overlooked by the patient or disregarded as unimportant. Delay by the patient in obtaining competent medical help remains one of the major factors contributing to the poor prognosis. A portion of the fault lies also with the physician, however. In these 96 cases there were 10 instances of a delay of over 1 month from the time medical consultation was sought until the diagnosis was made. In one case, over 24 months elapsed until the physician made the correct diagnosis. This patient survived 6 years.

TABLE II. SYMPTOMS

	NO. OF PATIENTS
1. Abdominal swelling	62
2. Abdominal pain	45
3. Gastrointestinal complaints	34
4. Genitourinary complaints	21
5. Weight loss	14
6. Backache	12
7. Menstrual irregularity	10
8. Pelvic mass	6
9. Other	11
10. None	2

Allan and Hertig[1] found that patients with symptoms of 6 months' duration or longer have a better prognosis because the metastatic rate is higher in those having symptoms for a shorter period. Our findings are in agreement with this observation, for of 25 patients who had symptoms for less than 3 months, 84 per cent were in Stages III and IV when the diagnosis was made and only 16 per cent were alive and well at the end of 5 years. Thirty-two patients had symptoms for 12 months or longer and, of these, only 66 per cent were in Stages III and IV when the diagnosis was made and 28 per cent survived 5 years or more (Tables III and IV).

The physical signs were of no more help than the symptoms in making an early diagnosis. Abdominal mass was the most common finding and was present in 45 per cent of the patients. In 41 per cent a pelvic mass could be found. Ascites was present in 21 per cent and was always indicative of far-advanced disease.

TABLE III. RELATIONSHIP OF DURATION OF SYMPTOMS TO LENGTH OF SURVIVAL

NO. OF PATIENTS	SYMPTOMS	SURVIVAL			
		0-6 MONTHS	6-12 MONTHS	1-5 YEARS	OVER 5 YEARS
5	Under 1 month	3		1	1
20	1-3 months	9	3	5	3
16	3-6 months	6	2	2	6
14	6-12 months	2	3	3	6
15	12-24 months	7	1	2	5
17	Over 24 months	4	3	6	4
8	Unknown	1	1	2	4
1	No symptoms				1

TABLE IV. RELATIONSHIP OF DURATION OF SYMPTOMS TO STAGE OF DISEASE

NO. OF PATIENTS	SYMPTOMS	STAGE			
		I	II	III	IV
5	Under 1 month	2	1	2	
20	1-3 months	1		11	8
16	3-6 months	2	1	8	5
14	6-12 months	3	4	5	2
15	12-24 months	4	1	4	6
17	Over 24 months	3	3	7	4
8	Unknown	3		3	2
1	No symptoms	1		1	

Pathology

All of the cases in this series were proved pathologically. Dr. Howard Gomes of the Department of Pathology has reviewed all the available slides for us and we have not included any case in which there was a possibility of the tumor being benign. In placing each tumor in a certain histopathologic type, we have attempted to follow the classification proposed by Novak,[14] but in some instances this has not been possible. Helsel[7] felt that it was unsatisfactory to attempt to classify these tumors as cystic or solid, as many that appear cystic have a solid core. The most common malignant ovarian tumor is the serous papillary cystadenocarcinoma. There were 54 such cases in this series, comprising 56 per cent of the total number of cases. Solid adenocarcinoma was next most common with 29 cases, or 30 per cent. There were fewer pseudomucinous cystadenocarcinomas than might be expected in a series of this size and the number of granulosa-cell carcinomas was greater than usual (Table V).

Comparison of the histopathologic type with the 5 year survival shows that 80 per cent of the patients who survived 5 years or longer had serous papillary cystadenocarcinoma, 10 per cent had solid adenocarcinoma, 6.2 per cent had granulosa-cell carcinoma, and 1 patient (3.1 per cent) had a malignant theca-cell tumor. All of the patients with solid adenocarcinomas who survived for 5 years or longer received postoperative radiation therapy.

Any attempt at placing these tumors in a grade of malignancy from I to IV would seem to be rather inaccurate because of the histopathologic variation in any single case. Our pathologist has, therefore, attempted to grade them as low, medium, or highly malignant tumors. By grading them in this manner and comparing the results with the 5 year survival, one finds that only 2 patients out of 30 (6 per cent), with tumors graded as highly malignant, survived for 5 years. Of the 14 cases graded as having low malignancy, 10 patients (31 per cent) survived for 5 years. One must remember, however, that nearly all those of low-grade malignancy were in Stage I or II while those of higher grades were in Stage III or IV when diagnosed.

TABLE V. HISTOLOGIC TYPES

	NO. OF PATIENTS
Serous papillary cystadenocarcinoma	54
Solid adenocarcinoma	29
Granulosa cell	4
Anaplastic carcinoma	4
Pseudomucinous cystadenocarcinoma	2
Theca cell	1
Malignant teratoma	1
Sarcoma	1
Total	96

The most important factor in the prognosis is not the histologic type or the grade of malignancy, but the gross stage of the disease at the time the diagnosis is made. The four stages proposed by Walter, Bachman, and Harris[24] of Mt. Sinai Hospital in New York have been used in this study. They are:

Stage I. Primary tumor, unilateral and completely removable, no visible metastases.

Stage II. Local metastases present, but completely removable with primary tumor so that no visible disease remains.

Stage III. Local metastases present, but only partially removable with primary tumor.

Stage IV. Cases with advanced carcinomatosis peritoneae in which only exploratory celiotomy or removal of large tumor masses may be performed as a diagnostic and palliative measure.

Surgical Treatment

Even in cases thought to be inoperable, surgery is indicated in order to make a diagnosis and also because of the possibility that all of the malignant growth may be removed. When it is found to be inoperable a biopsy should be obtained. Parks[15] has reported 3 cases of inoperable papillary cystadenocarcinoma which were made operable by the use of adequate radiation therapy. Diddle[4] also believes that in a few instances preoperative radiation may make an inoperable tumor operable. This procedure is condemned, of course, unless a definite histologic diagnosis is made first.

The primary growth should be removed even when the disease has spread beyond the ovary. Swinton and Yancey[20] believe that all patients with ovarian cystic tumors 7 cm. or more in diameter should be carefully observed. If the tumor persists, an exploratory operation should be performed. Wherever possible, the surgery of choice is bilateral salpingo-oophorectomy with total hysterectomy. In our patients who survived over 5 years, 59 per cent were treated either by total hysterectomy and bilateral salpingo-oophorectomy (4 cases) or by subtotal hysterectomy and bilateral salpingo-oophorectomy (15 cases).

During the operation it is important that no cyst be ruptured. Every cystic or solid tumor of the ovary that is removed should be opened by the surgeon before the wound in the abdomen is closed. If carcinoma is reported later by the pathologist in an unsuspected case, the patient should be reoperated upon. The surgeon should not take too great a risk in an attempt to remove all fragments of diseased tissue. He should do what can be done easily and then rely on x-ray therapy in adequate dosage. The removal of as much of the visible neoplastic tissue as possible reduces the amount of toxic material to be absorbed following irradiation. Pemberton[16] and Meigs[12] feel that it is important to remove the omentum also.

Radiation Therapy

Kerr and Einstein[8] begin radiation as soon after surgery as the patient's condition permits in order to decrease the formation of fluid. This, they feel, is especially important in cases with ascites. On the other hand, Freed and Pendergrass[6] wait 6 weeks in order to give the patient a chance to recover from the surgery. If the patient's condition deteriorates during this time, they feel that she would not have responded well to radiation therapy anyway. In this series, treatments were usually begun 1 to 2 weeks following surgery. The physical factors consisted of 200 kv., 15 ma., 50 cm. target skin distance, and 0.5 to 1.0 mm. of copper filter (half-value layer 1.07 to 1.60 mm. of copper).

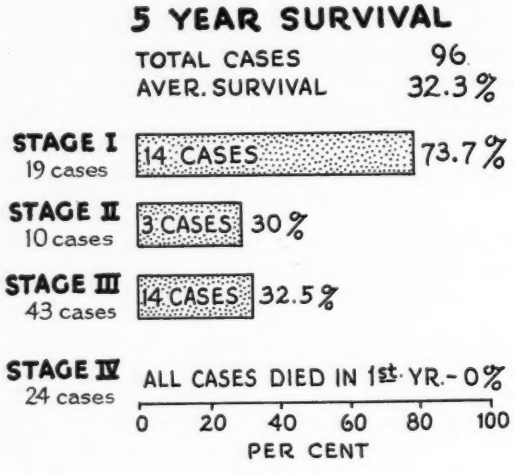

Fig. 1.

There was no great degree of uniformity in the portal size or the number of roentgens given daily. In general, however, 2 anterior and 2 posterior 10 by 15 cm. fields were employed with lateral or sciatic fields used also in approximately 25 per cent of the cases. The number of 5 year survivals was slightly higher in those patients who had the additional lateral or sciatic fields, suggesting some possible benefit from their use. Doses of 200 r (air) to each of 2 fields for 5 days a week were commonly given. However, doses consisting of from 150 to 300 r daily to 2 fields, or 200 r daily to one 10 by 20 cm. field were used occasionally without significant difference in the survival rate. Each field was given a total of from 2,000 to 2,400 r (air), the exact amount being determined in each case by the patient's tolerance of the treatment and by her general condition.

The total dosage was given in from 3 to 8 weeks, the average being about 5 weeks. No difference in survival rate was noted between those who received a rather short intensive course of treatment over 3 weeks and those who received a prolonged series over a period of 8 weeks.

One patient who had a bilateral solid adenocarcinoma, Stage III, received only 850 r (air) to four 10 by 15 cm. fields over a period of 4 months. Even with this admittedly inadequate treatment, she survived 5 years before she died of metastases.

In 4 cases an additional course of treatment was given after several months utilizing sciatic, oblique, or lateral fields which had had no previous treatment. Of these 4 patients, one in Stage II is well at 7 years; one patient in Stage III is alive with disease at 6 years; and the other 2, who were also in Stage III, lived 5 and 30 months, respectively.

Results

In estimating the results we have kept in mind the main purpose of this study as stated previously—that of comparing the results of surgical treatment alone with those of surgery plus postoperative irradiation in various stages of ovarian malignancy. At this institution, many cases have been treated by surgery alone in the past, thus affording a fairly representative group of cases treated by either method.

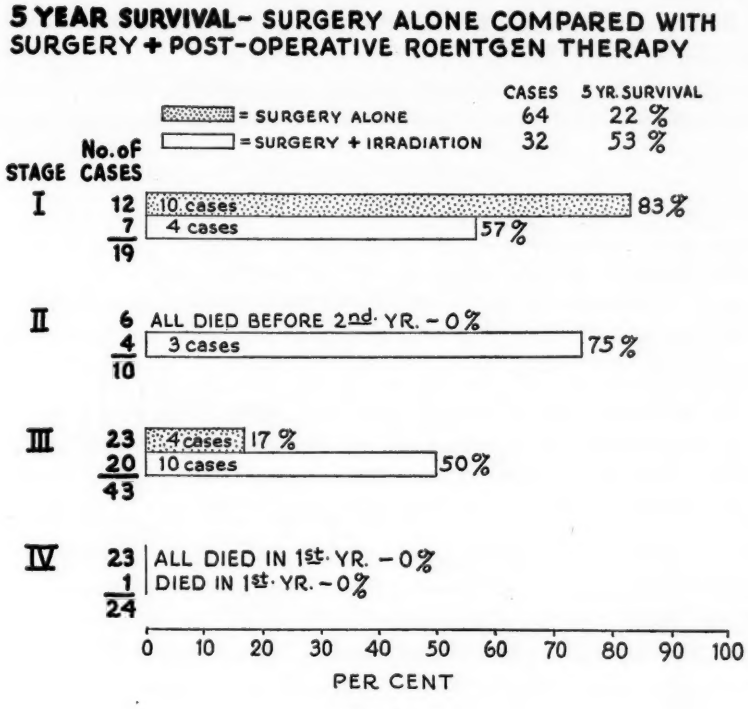

Fig. 2.

The results of treatment in the 96 cases are seen in Fig. 1. The over-all 5 year survival rate was 32.3 per cent. The number of patients in each stage and the number who survived for 5 years are also shown. Most of the cases were in the advanced stages when first seen. The rapid decrease in survival after the tumor has spread beyond the ovary is well shown by the decrease in the 5 year survivals from 73.7 per cent in Stage I to 30 per cent in Stage II. It is also worthy of note that all the patients in Stage IV died within 1 year after the diagnosis was made.

In Fig. 2 the cases in each stage have been separated into those treated by surgery alone and those which received postoperative radiation therapy. The over-all 5 year survival for patients treated by surgery alone is 22 per cent and for those treated by surgery plus postoperative irradiation it is 53 per cent.

The excellent survival rate of 83 per cent of Stage I cases treated by surgery alone probably cannot be improved by the addition of radiation therapy. Mention might be made, however, of the 57 per cent survival rate in those Stage I cases given postoperative irradiation. The great discrepancy in the results of the two methods of treatment would be markedly reduced if one patient who died after 2 years of meningitis and another who died of pulmonary embolus after 3 years were omitted from the group treated with radiation. The results would then be very nearly equal—80 per cent and 83 per cent.

The small number of cases treated by each method in Stage II is probably not of statistical value. However, the marked difference in the survival rate of the patients treated by each method seems to indicate that postoperative irradiation is definitely of value in this group.

Approximately one-half of the 43 cases in Stage III were given postoperative irradiation. The difference in the 5 year survival in this group is striking and significant. With surgery alone, only 17 per cent survived 5 years. The addition of radiation therapy in this group increased the survival rate to 50 per cent. This is a difference in the 5 year survival rate of 33 per cent.

All but one of the cases in Stage IV were treated by surgery alone, so no estimate as to the value of irradiation in this stage can be made. It is apparent, however, that surgery alone has little to offer this large group of patients.

Long-Term Survivals

The distribution of the patients who have been treated by each method and who have survived over 5 years is shown in Tables VI and VII. The good results in the Stage I cases treated by either method are evident. Six of the 7 patients who survived 10 years or longer are alive and apparently free of disease at the present time. Those Stage III cases given postoperative irradiation apparently have a much better chance for survival as can be seen by comparing the number of long-term survivals in the two groups. The single 16 year survival of a patient in Stage III treated by surgery alone cannot be explained, as widespread metastases in the abdomen were noted at the time of surgery. There has been reported, at times, regression of metastases following removal of a primary tumor, and this may be an example of such a case.

TABLE VI. LONG-TERM FOLLOW-UP WITH SURGERY ALONE

NO. PATIENTS	STAGE	YEARS											
		5	6	7	8	9	10	11	12	13	14	15	16
10	I		1		3†	2*	1		2‡	1*			
0	II												
4	III	2*		1									1*
0	IV												

*One patient free of disease in 1954.
†One patient died of generalized arteriosclerosis.
‡Both patients free of disease in 1954.

TABLE VII. LONG-TERM FOLLOW-UP WITH SURGERY PLUS X-RAY

NO. PATIENTS	STAGE	YEARS											
		5	6	7	8	9	10	11	12	13	14	15	16
4	I				1*		1*	1*	1*				
3	II			2*				1*					
10	III	1	4*	1*	1†			1‡	1*	1*			
0	IV												

*One patient free of disease in 1954.
†One died of pulmonary embolus with no evidence of tumor at autopsy.
‡Alive with disease.

Comment

Opinions differ somewhat as to the amount of relief afforded patients who are given postoperative irradiation. The many encouraging reports which have appeared from time to time in the literature seem to leave little room for doubt that surgery followed by irradiation gives definitely superior results to surgery

alone in those cases in which the tumor is not entirely localized to one ovary.[1, 2, 3, 5-11, 24, 28, 30, 31, 35, 36, 37] While some feel that life is prolonged, others maintain that life, though not prolonged, is made more comfortable by reducing the rapidity with which ascitic fluid is re-formed. Pemberton[16] and Allan and Hertig[1] found in their series that longevity was increased and the life of the patient made more tolerable, but they did not feel that the use of radiation cured the disease.

Opinion is still divided as to the value of postoperative irradiation in Stage I. Marks and Wittenborg,[10] Kerr and Elkins,[9] and Schmitz and Majewski[19] have published series in which *all* patients with ovarian malignancy were given postoperative radiation. Others feel that when the disease is entirely localized to one ovary (Stage I) surgery alone gives as good results as any other method.[6, 12, 24] This has been true in the series reported here. Munnell and Taylor[13] advocate treating all cases with radiation after surgery, except those of low-grade malignancy in Stage I.

At the present time only a few authors feel that postoperative radiation has little or nothing to contribute to the treatment of ovarian malignancy. Taylor and Greeley[21] state that in their series of 26 patients who received "adequate" radiation, no increase in the average duration of life could be found when compared with the duration in 82 patients treated by surgery alone. In their report, those patients who received "650 r or more per port in a single treatment or a series of small treatments totaling 1,500 r or more" were counted as having "adequate" radiation. Undoubtedly, many of these patients received inadequate radiation by standards in use today. Diddle[4] states that the formation of ascites is retarded and intra-abdominal implants grow more slowly following the use of irradiation. He also feels that life is occasionally prolonged by its use. Te Linde[22] does not believe that routine postoperative radiation is justified by the statistical results available.

Summary and Conclusion

1. A series of 96 proved cases of carcinoma of the ovary has been reviewed primarily for the purpose of evaluating therapeutic results. The survival rate in this group was 32.3 per cent.

2. Most cases are still being diagnosed only in the advanced stages and the survival rate has remained quite constant for a number of years.

3. The stage of the disease is the most important factor affecting prognosis. The histopathologic type and the grade of malignancy are contributing, but less important, features.

4. Of 64 patients treated by surgery alone, 22 per cent were alive at the end of 5 years and most of these were originally in Stage I. Surgery should consist of a minimum of total hysterectomy and bilateral salpingo-oophorectomy.

5. Thirty-two patients were given postoperative radiation and of these 53 per cent were alive at the end of 5 years. Most of these cases were in Stage III when diagnosed.

6. From these results it appears that postoperative irradiation, given in adequate dosage, definitely increases the survival rate of patients in whom all the tumor cannot be removed at surgery.

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METASTATIC CARCINOID TUMOR OF THE OVARY

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CARCINOID tumors of the female generative tract are rare. A brief review of their salient pathological and clinical characteristics is therefore presented prior to reporting the case noted here. The designation carcinoid tumor is indeed in itself a paradox. As first coined by Obendorfer in 1907 it was meant to indicate a specific tumor of the intestinal tract with malignant histological characteristics, but which seemingly followed a benign clinical course. It was soon apparent, however, that in spite of their slow growth and prolonged localization, carcinoid tumors ultimately become invasive and produce both local and distant metastases.

Carcinoid tumors are derived from specific granular cells lying in the crypts of Lieberkühn, i.e., the Kultschitsky cells, named after their first observer. The cytoplasm of these cells as demonstrated by Gosset and Masson shows special chemical affinity for silver and chromium salts. Because of this property, carcinoids are interchangeably designated as argentaffin tumors. Their high lipid content, however, allows their differentiation from other chromatin cells which also reduce silver compounds. A clearer insight into this specific cell-staining property was advanced by Erspamer, who hypothesized the presence of "enteromin" in the cytoplasmic granules of the tumor cells. Chemically, Gomari noted that either resorcinol or a related phenolic compound in the granules is the actual causative agent in the silver reduction.

Though carcinoid tumors have been found in the respiratory tract and even in the nasal mucosa (Simard and Jean), they arise almost exclusively in the mucous membrane of the gastrointestinal system. The appendix is the seat of predilection, and Dockerty and associates record an incidence of 0.5 per cent of carcinoids in all surgically removed appendices. The ileum is the next most frequent location. Thus Pearson and Fitzgerald record a ratio of 70 appendiceal carcinoids to 19.4 ileal carcinoids in their series of 140 cases. The jejunum is the third site in order of frequency. They are least often encountered in the colon. Of 14 tumors of the colon, Stout found 4 in the cecum and 10 in the other segments of the colon. He also described 5 carcinoids of the rectum, which, however, failed to reduce silver, and accordingly ascribed their derivation to "Erspamer's pre-enterochrome cells." Epps and his associates collected 72 carcinoids of the rectum and emphasized their favored seat on the anterior rectal wall 5 to 10 cm. above the anus. Such rectal tumors, therefore, are occasionally detected during routine vaginal examination, as in Case 1 and Case 3 of Warner's short series. Willis has found carcinoids in the stomach, gall bladder, and even in a Meckel's diverticulum.

Multiple primary lesions are the rule. Dockerty and Ashburn reported such manifestations in one-third of their cases. Cooke reported multiple tumors in 27 of 76 cases obtained by operation or autopsy. In the small bowel, Willis has encountered 20 to 60 neoplasms in one specimen, in addition to numerous nests first revealed by microscopic examination. In all locations, carcinoids begin as nodules or plaques in or beneath the mucosa, and soon bulge into the lumen. The yellow or orange color is distinctive. Advanced lesions encircle the bowel and cause infolding of the muscularis. In the appendix, the distal tip is generally the seat of the tumor, which presents as a firm solitary nodule possibly reaching 1 to 2 cm. in diameter. On cut section through the tumor site, the lumen of the appendix is often obliterated. Yellow-gray or yellow-brown tissue occupies the mucosa, submucosa, and muscularis, although the latter often remains identifiable.

Microscopically, enteric, colonic, and appendiceal carcinoids present similar morphology. The tumor cells are variously arranged in cords, alveoli, or in festooned ribbons. Rosette types, palisade columns, and irregular insular cell masses may be present. Willis reported cases with definite glandular lumina and clear-cut acini. The individual cell is demarcated by a cell membrane. It is small in size and is generally spheroidal or polyhedral in contour. Low columnar and cuboidal forms are reported by Warner. The round or oval, and occasionally elongated, nucleus stains deeply and is centrally placed. The chromatin granules are fine and evenly distributed. Mitotic figures are rare. The cell cytoplasm is scant, finely granular, and faintly acidophilic. Vacuolization is not uncommon. Cholesterol and mucin are demonstrable by special stain. The classical argentaffin granules are demonstrable as a rule by the Masson-Fontana technique. The supporting stroma is comprised of hyaline connective tissue. The usual morphological criteria for malignancy are established with difficulty, for even in the heterotopic nests of the invaded bowel wall or in metastases the cells are uniform and mitotic figures infrequent. Nuclear aberrations in size, contour, and staining intensity are infrequently noted.

The biological behavior of carcinoid tumors is unique. Slow growth and prolonged localization differentiate this neoplasm from all other carcinomas, justifying the misnomer "carcinoid tumor" as proposed by Obendorfer. Mallory reported an ileal carcinoid with known metastases for 20 years, death ultimately resulting from intercurrent pneumonia. Though Pearson and Fitzgerald reported 90 cases of appendiceal carcinoid without local or systemic spread, 16 of their intestinal carcinoids showed metastases distributed variously in the mesentery, liver, intestinal serosa, omentum, distant lymph nodes, and the vertebrae. Ritchie and Stafford collected 23 appendiceal carcinoids with either regional or distant metastases. Willis noted metastases to the lungs, adrenal glands, brain, and retroperitoneal tissues.

Clinically, carcinoid tumors occur most frequently in middle life or old age. In the small intestines the tumor is often first revealed at operation, which is necessitated by symptoms of partial or complete obstruction. Many cases remain locally asymptomatic. Rectal lesions may produce bleeding. The

favored site of carcinoids, on the anterior rectal wall and within 10 cm. from the anus, may allow their detection by rectal examination even if symptoms are lacking. Appendiceal lesions are generally latent and most often are accidentally disclosed at operation or autopsy. In the case reported here, the primary appendiceal site was found only at autopsy, the hepatic and especially the ovarian metastatic lesions having dominated the clinical picture. Compared to other malignant lesions, carcinoid tumors present a relatively favorable prognosis. In appendiceal cases, even with local nodal invasion, appendectomy and excision of the involved lymph nodes will, according to Willis, afford a surgical cure. Pearson and Fitzgerald also deem excision of the local lesion and regional metastases advisable in patients with a reasonably long life span. It must be mentioned, however, that in the 140 cases reported by Pearson and Fitzgerald, 23 also presented a second primary malignancy of different histogenesis.

Though carcinoid tumors of the appendix are not infrequently encountered in gynecological surgery of the pelvis and lower abdomen, the exact incidence is generally unrecorded. Grunstein and Barrows, however, reported an appendiceal carcinoid coincidentally with a Brenner tumor of the right ovary and a pseudomucinous cystadenoma and fibroma of the left ovary. In April, 1951, Helwig presented a left-sided ovarian tumor, which, though friable and necrotic, was basically of solid texture. Yellow-gray and gray-white foci of tumor tissue presented at the periphery. The appendix simultaneously removed contained a yellow nodule at the obliterated tip which measured 3 mm. in diameter. After microscopic study of hematoxylin and eosin sections, the author could not decide whether this case represented a primary appendiceal carcinoid with secondary metastases to the ovary, a granulosa-cell tumor with secondary extension to the appendix, or whether these two lesions presented simultaneously and independently; for both neoplasms reproduced a pattern suggesting folliculoid granulosa-cell tumor. Silver stains, however, showed characteristic black granules only in the appendiceal tissue indicating the coincidence of the two lesions.

Six cases of primary ovarian carcinoids have been reported to date. All have been associated with cystic teratomas of the ovary. This is readily understandable, for segments of the intestinal tract are often reproduced in these neoplasms. Mitchell and Diamond, who reported the sixth case, found multiple argentaffin tumors in the interior of a cystic teratoma 12 cm. in diameter. These were associated with derivatives from the respiratory tract. Reviewing the 5 earlier cases on record, the same authors showed that 2 contained derivatives of the gastrointestinal tract in association with carcinoids. Two others, though lacking a distinctive intestinal mucosa, nevertheless showed the muscle layers. Mucus-secreting glands and hyaline cartilage in the same cases indicated the presence of derivatives from the respiratory system. In the fifth case, both intestinal and bronchial elements were in close association with carcinoid nodules lying adjacent to ciliated lining epithelium and glands. It should be emphasized, however, that both systems are of entodermal origin and the presence of carcinoids in both is therefore understandable.

The third group of carcinoid tumors in the female generative tract is metastatic in origin. Epps and co-workers in 1949 found a primary rectal carcinoid with a metastasis to the left broad ligament. The metastatic lesion had been erroneously regarded as an enlarged left ovary over a four-year observation period. At operation, it presented as an easily removable parametrial tumor, 4 by 4 by 5 cm. in diameter. Interestingly, too, the pathological diagnosis ranged from granulosa-cell tumor, to low-grade carcinoma of either Wolffian- or Müllerian-duct origin. One observer, however, suggested the intestine as the primary site. A belated proctoscopic study showed a carcinoid tumor located in the anterior rectal wall, within 6 to 8 cm. of the anus. Sections from the growth showed cords, strands, and festoons of low columnar and cuboidal cells with uniform nuclei. Double rows of cells were classically encountered in many festooned ribbons.

The case which follows demonstrates the difficulty in the differential diagnosis between a primary granulosa-cell tumor of the ovary and a metastatic carcinoid of appendiceal origin.

Mrs. E. H., aged 60 years, was admitted to the service of Dr. William A. Jewett at the Long Island College Hospital, on May 8, 1940, with complaints of diarrhea and heaviness in the abdomen for the past eight months. The previous medical and surgical history was irrelevant. Two confinements, 32 and 30 years before, were without incident. Curettage and insertion of radium for endometrial hyperplasia (diagnosis confirmed) were performed in 1929, and were followed by permanent amenorrhea. The present illness began in October, 1939, with a sensation of pressure in the lower abdomen, associated with a daily evacuation of 4 to 5 watery stools. A weight loss of 10 pounds had occurred during this interval. The pertinent physical findings were limited to the abdomen and pelvis. The former was distended by a tumor reaching from the pelvis to the level of the umbilicus, and encroaching upon the right iliac and right paraumbilical zones. The neoplasm was firm, nodular, insensitive, and only partially mobile. A second tumor mass occupied the right upper quadrant and was seemingly connected with the enlarged liver. Dullness in the flanks and a fluid wave were both present. Vaginal examination showed a normal marital introitus. The cervix and uterus were atrophic. The body of the uterus was fused with the lower abdominal tumor previously noted. Laboratory data were nonrevealing. A flat plate of the abdomen confirmed the two tumor masses clinically described. The liver was noted as enlarged and a calcified lymph node was detected in the right lower abdomen. A diagnosis of carcinoma of the right ovary, with intraabdominal and hepatic metastases, was made and confirmed by laparotomy on May 18, 1940. About 2,000 c.c. of blood-tinged fluid was found free in the abdominal cavity. The liver was enlarged and the seat of numerous metastases involving both lobes. The uterus and left adnexa were normal. The right tube was elongated. The right ovary was the seat of an ovoid tumor about 12 cm. in diameter. The omentum, mesentery, and intestines were free from metastases. Because of the advanced stage of the disease, only a right salpingo-oophorectomy was performed. The immediate postoperative course was uneventful.

The pathological examination of the right adnexa showed a normal tube measuring 40 mm. in length and 5 mm. transversely. The right ovary was converted into a solid ovoid tumefaction, 15 by 14 by 12 cm. Externally it was gray white in color. On cut section, a fibrous reticulum was prominent and its meshes were infiltrated with soft yellow tumor material. Areas of liquefaction were numerous. Remote from these zones, however, the broad fibrous trabeculae often encased minute cystic spaces, thus reproducing the pattern of a fine honeycomb. Microscopically, the connective tissue was prominent and largely hyalinized. It subdivided the tumor into large and small tumor alveoli, which had retracted from the adjacent stroma. Central necrosis, with resultant cavitation, was prominent in many alveoli

(Fig. 1). In some areas, cavitation was so pronounced that a relatively large central cavity was surrounded by only a narrow zone of tumor cells (Fig. 2). Throughout the tumor, the cell pattern was uniform. The cells were of small size, round or polyhedral in shape, with a well-defined cell membrane. The cytoplasm was clear, granular, and often vacuolated. The nuclei were central in position, vesicular in character, round or ovoid in form. The chromatin

Fig. 1.

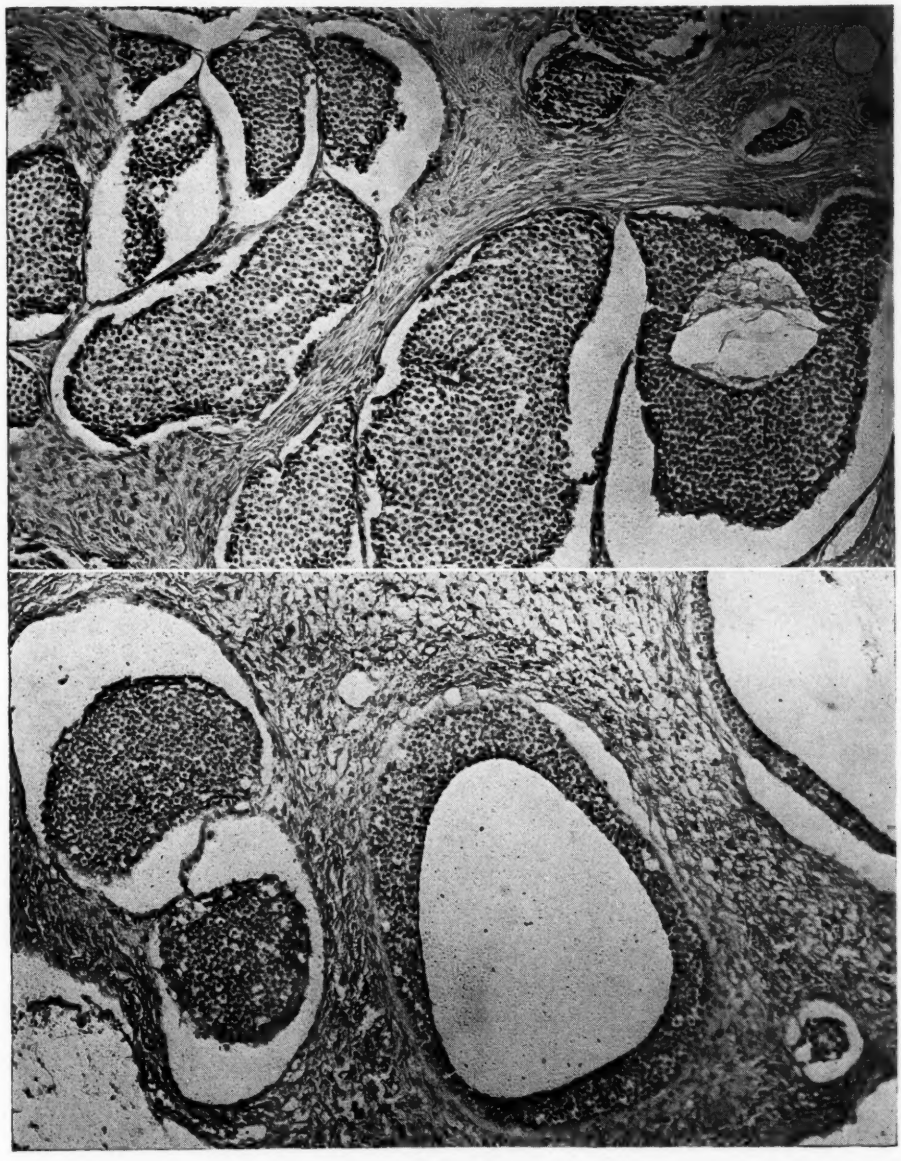

Fig. 2.

Fig. 1.—Ovary. The tumor is comprised of large and small alveoli which have retracted from the adjacent compact hyalinized stroma. The individual cell is small, round or polyhedral in form. The cell membrane is distinct, the cytoplasm clear, and the central nucleus vesicular in type. Cavitation is present in the alveolus on the right. (×120; reduced ¼.)

Fig. 2.—Ovary. Note the cystic spaces lined by 4 to 10 layers of epithelial cells. The follicular form of granulosa cell is imitated. Liquefaction in the cell column even imitates early Call-Exner bodies. However, the circumferential arrangement of the basal-cell layer present in granulosa-cell tumors is lacking. The relatively abundant cell cytoplasm and the sharp cell membrane should be noted. (×120; reduced ¼.)

was uniformly distributed, although in many cells nucleoli were common. Mitotic figures were not observed. Irregularity of nuclei was uncommon. About the cystic spaces, surrounded by 4 to 10 layers of tumor cells, hydropic degeneration of cells was frequent. Liquefaction of contiguous cells often reproduced the pattern of Call-Exner bodies, but cell radiation was lacking. Sudan III stains showed fat droplets of varying size located in the cell bodies, and

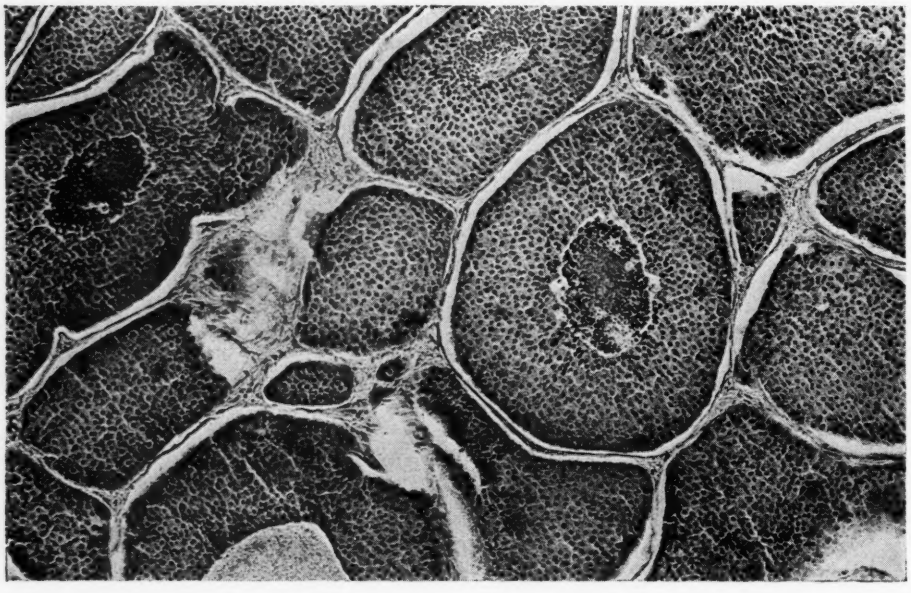

Fig. 3.—Metastatic lesion in the liver. Note the large tumor alveoli and the well-defined connective tissue septa. The cells present the same characteristics as in Figs. 1 and 2. However, variation in size, contour, and staining of the nuclei is apparent. (×120; reduced ¼.)

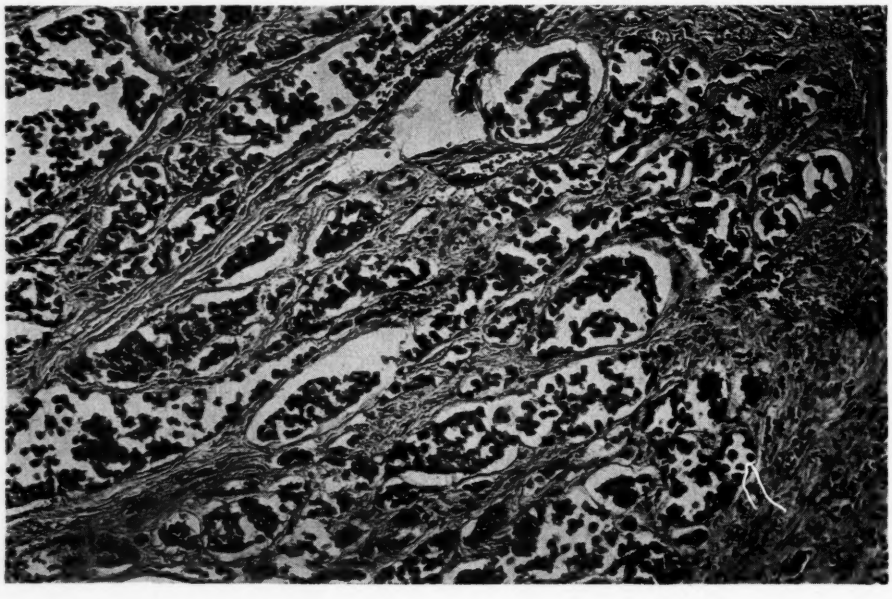

Fig. 4.—Primary lesion in the appendix. Nests, cords, acini, and irregular glands are demarcated by a prominent fibrous stroma. The cell remains small. The nucelus, however, is larger and more deeply staining than in the ovarian lesion, and the cytoplasm is less prominent. (×120; reduced ¼.)

larger collections lying free between the tumor cells. A diagnosis of granulosa-cell tumor, with focal luteinization, was made. The uniform cell pattern seemingly belied the malignant behavior revealed by metastases to the liver. The slides were accordingly submitted to four consultant pathologists. Two confirmed the diagnosis of granulosa-cell tumor. The third suggested a metastatic ovarian lesion, secondary to myeloma. The fourth believed the lesion a metastatic carcinoid of the ovary.

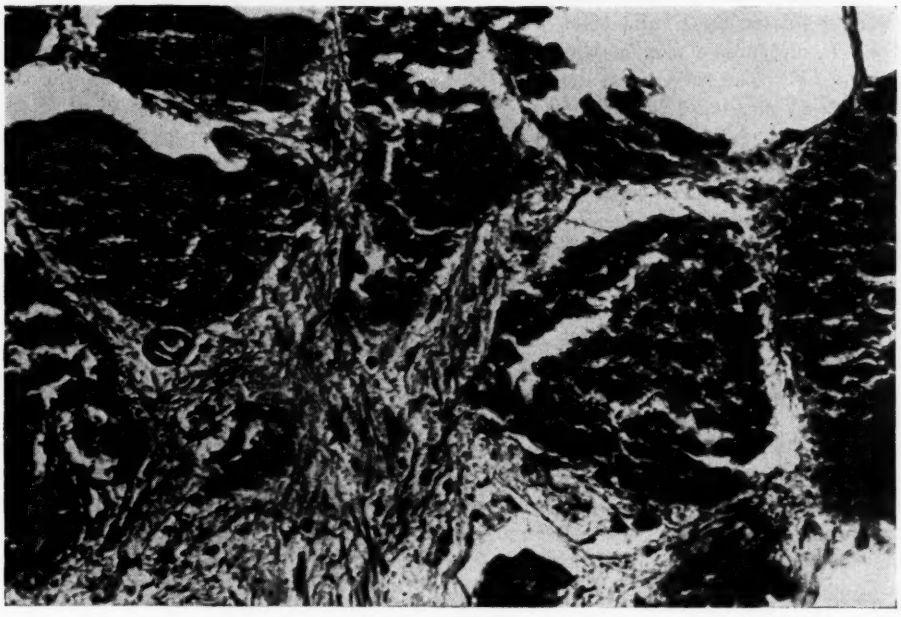

Fig. 5.—Ovary. Masson-Fontana stains reveal argentaffin granules within the cell cytoplasm. This is well shown in the cell cord on the right. (×375; reduced ¼.)

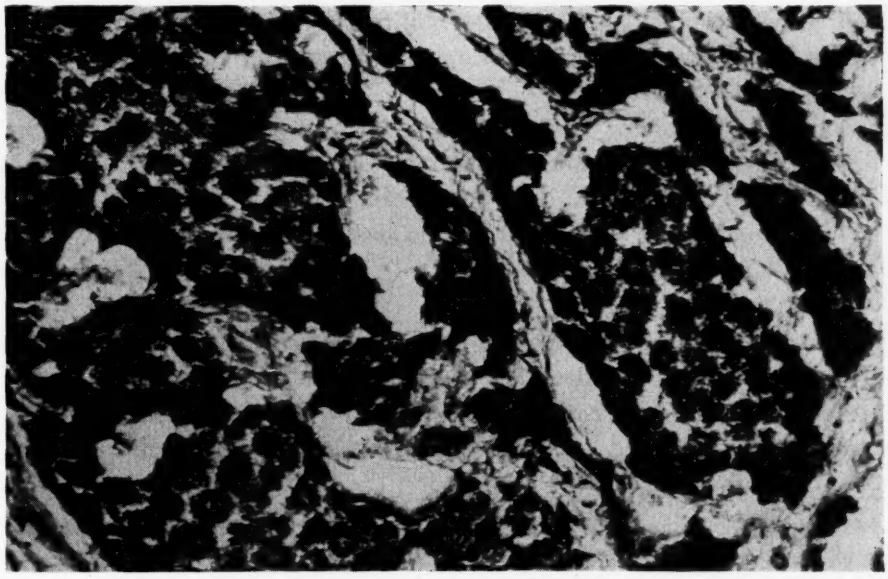

Fig. 6.—Liver. Argentaffin granules are well shown in practically all cells by the Masson-Fontana stain. (×375; reduced ¼.)

The condition of the patient deteriorated progressively, and death occurred at the Mountain Lake Hospital, Montclair, New Jersey, on Nov. 7, 1940. Autopsy consent limited to exploration of the abdominal and pelvic cavities was obtained. The liver and the intestines, after removal, were forwarded to the Hoagland Laboratory for search for a primary intestinal tumor. The gall bladder was grossly normal. The enlarged liver presented multiple metastases in both lobes, ranging from 5 to 50 mm. in diameter, the largest tumor presenting on the anterior aspect of the right lobe. The liver parenchyma adjacent to the tumors showed congestion and fatty infiltration. The tumor nodules presented a striking yellow color. The duodenum, jejunum, ileum, and colon were all normal. The appendix, however, was firm and cordlike. It measured 6 cm. in length and 8 mm. transversely at the cecal junction, and 4 mm. at the tip. The serosa was smooth. Multiple sections showed complete obliteration of the lumen. At the base, however, pinhead-sized yellow flecks of tissue could be discerned throughout all layers. The lymph node at the junction of the mesoappendix and cecum was calcified and measured 15 by 10 mm. Microscopically, multiple sections from the liver showed the tumor comprised of moderate-sized round, ovoid, or cylindrical alveoli (Fig. 3). The component cells were small, and presented a definite membrane. The nuclei were of vesicular type, surrounded by a moderate amount of faintly staining granular cytoplasm. Many showed variation in size and contour and others stained deeply. Sections from the appendix revealed chronic obliterative appendicitis. Near the base, the central fibrous core contained minute yellow islands of tumor tissue, which invaded the muscularis and reached to the serosa. The nests of tumor cells were everywhere encased in hyaline connective tissue. Microscopically, they presented in strands, acini, and atypical glands. As in the ovary and liver, the cell was small in size, round or spheroidal in contour, but with a less distinct cell membrane. The cytoplasm, too, was reduced in amount, and the nuclei relatively larger, more deeply staining, and often irregular in contour. Mitotic figures were not observed. The calcified lymph in the mesoappendix showed similar cords and alveoli of neoplastic cells. By the Masson-Fontana technique, sections from both the ovarian and hepatic tumors presented black-brown argentaffin granules in their cytoplasm, indicating their common origin from the appendiceal carcinoid (Figs. 5 and 6).

Summary

1. The histology, pathology, and clinical behavior of carcinoid tumors of the intestinal tract have been reviewed. Their slow growth and relative benignancy are stressed. Chemically, the ability of carcinoid cells to reduce silver compounds is a specific diagnostic characteristic earning for them the alternate designation of argentaffin tumors.

2. Carcinoid tumors of the female genital organs are rare. A primary form, associated with cystic teratomas containing segments of the gastrointestinal or respiratory tract, or both, has been recorded.

3. The secondary or metastatic form is even more uncommon. A metastatic ovarian and hepatic carcinoid, secondary to an appendiceal tumor, is herein reported.

4. Ovarian tumors occurring coincidentally with appendiceal carcinoids present problems in diagnosis of the primary origin of the neoplasm.

5. The microscopic resemblance of carcinoid tumors to granulosa-cell neoplasms has been indicated. The Masson-Fontana stain is decisive in making the true differential diagnosis.

Addendum.—Since the preparation of this manuscript, Thorson and associates reported a series of carcinoids of the small intestine with metastases to the liver, valvular disease of the right heart, peripheral vasomotor symptoms, bronchial constriction, and unusual cyanosis. Of 16 cases comprising this series, 6 occurred in women. All presented metastatic carcinoid

lesions to one or both ovaries. The authors believe that enteramine of Erspamer elaborated by carcinoids is related to 5 hydroxytryptamine. It is the causative vasoactive factor accounting for the vascular changes (both peripheral and pulmonary) which ultimately cause the lesions of the right side of the heart, as well as the peculiar red flushing of the skin and the patchy changing cyanosis.

My sincere thanks are expressed to Mr. Steve Montis for his excellent photomicrographs and to Miss Audrey J. Stack for her technical assistance with the Masson-Fontana stains.

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GYNECOGRAPHY SIMPLIFIED*

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GYNECOGRAPHY, a term introduced by Stein, includes the visualization of the uterus, tubes, and ovaries by means of pneumoperitoneum plus hysterosalpingography. This technique, which permits an accurate diagnosis of obscure pelvic pathology, has been utilized successfully in many thousands of patients during the past twenty-five years by Dr. Stein and his group[1, 2, 3] at Michael Reese Hospital. His group has improved the method originally suggested by Jacobaeus[4] in 1912. Others who have reported on this procedure include Weber,[5] Lorey,[6] Stein and Stewart,[7] Alvarez,[8] and Peterson.[9]

In 1929, Stein and Arens[10] designed a special radiographic table which facilitated placing the subject in a modified knee-chest position. This table, though simple in construction, was never available commercially. In recent years, Stein and Arens[11] were able to employ a modified Sisk urologic table. While this new table has the distinct advantage that it can be used by both the urologist and the gynecologist for roentgen diagnosis, it is expensive special equipment, and, as such, cannot be recommended for the small hospital or private practitioner. We have utilized the ordinary x-ray table, tilted down 15 degrees, and placed a 4 inch thick pad on the table in such a manner that the patient can be placed in position for proper x-ray exposure. We have taken numerous films with standard x-ray equipment and have obtained excellent results. The purpose of this paper is to show that good gynecography can be done by utilizing any standard x-ray equipment. It is our hope that with the aid of the following simplified technique, the practitioner will avail himself more extensively of this diagnostic aid.

Gynecography is valuable (1) whenever the usual method of bimanual examination is inconclusive; (2) when the patient has been given conflicting opinions by various physicians; (3) for complete pelvic survey in patients complaining of infertility; (4) for the differential diagnosis in cases of suspected unruptured ectopic pregnancy; (5) in the obese woman; (6) where only rectal examination is possible; (7) for diagnosis of ovarian pathology such as bilateral polycystic ovaries associated with amenorrhea and sterility (Stein-Leventhal syndrome); (8) in developmental anomalies of the uterus and appendages such as septate, bicornuate, or double uterus; (9) for the

*Presented at a meeting of the Chicago Gynecological Society, Jan. 15, 1954.

establishment of the existence of the internal female genitals in pseudohermaphroditism. In addition, the films become a permanent record, available not only for comparison, but for multiple opinions as well.

Technique

1. For clear visualization of the pelvic viscera, the lower bowel is emptied by an enema the morning of the examination, or by cathartic the preceding night. A mild sedative such as 50 mg. of Demerol should be given one-half hour before the examination to prevent tubal spasm and to control the moderate amount of discomfort incidental to gaseous distention of the peritoneal cavity. The urinary bladder must be catheterized immediately before the examination.

2. Gas must be introduced into the peritoneal cavity (pneumoperitoneum) to silhouette the pelvic organs, and to displace the bowel. This can be done by the transuterine route in the same manner as the usual gas patency (Rubin) test, but it is more simply accomplished through the anterior abdominal wall. We prefer the transabdominal injection of carbon dioxide gas since it is the easiest and most rapid method of effecting pneumoperitoneum.

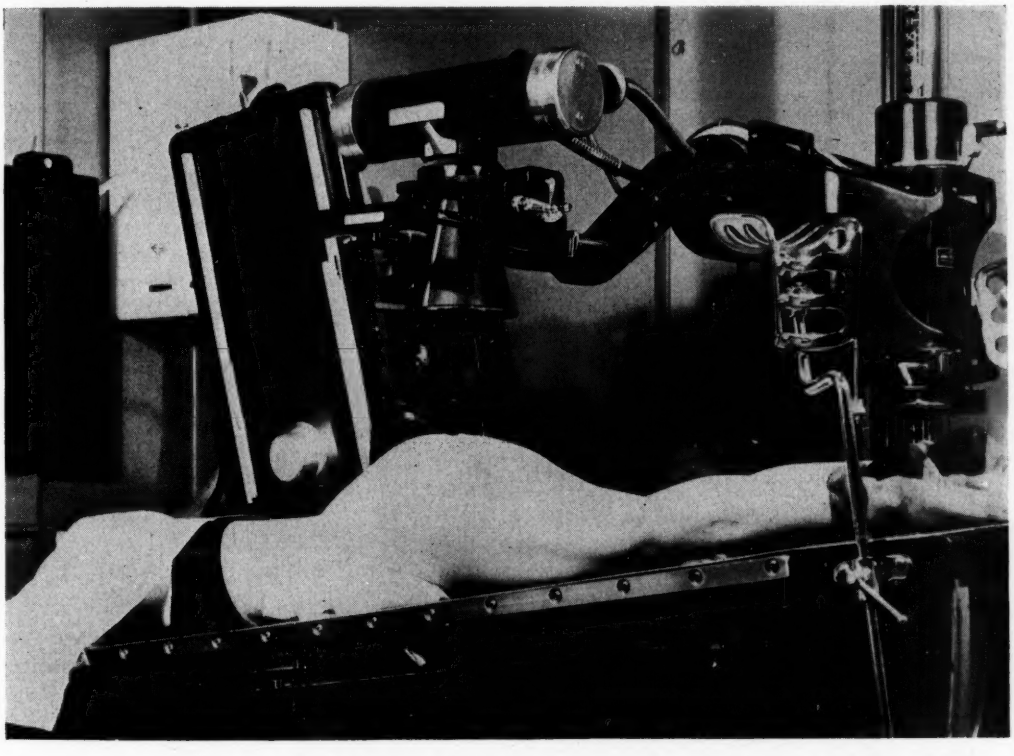

Fig. 1.—Patient in position on x-ray table. The head is canted down 15 degrees.

Pneumoperitoneum by the transuterine route is similar to the gas patency (Rubin) test. Carbon dioxide is the gas of choice, but instead of injecting only a few cubic centimeters of gas to establish the diagnosis of tubal patency, a measured quantity averaging 1,000 c.c. is injected intraperitoneally. Carbon dioxide is introduced under controlled pressure, which is not to exceed 180 mm. mercury, and is measured by means of a water-displacing volume meter. Any suitable uterine cannula may be employed.

In pneumoperitoneum by the transabdominal route, the patient is placed in the dorsal position, somewhat extended by elevating the hips on a 4 inch thick pad. A large bore (No. 18) spinal needle is inserted 1 inch below the umbilicus and one-inch to the left of the midline through the skin, fascia and muscle, and peritoneum. Carbon dioxide is injected under pressure not higher than 40 mm. of mercury. If the pressure exceeds this limit, the gas is being injected subperitoneally, and this will cause severe abdominal pain. It is necessary, therefore, to stop and readjust the spinal needle. Unless the gas is injected intraperitoneally, no visualization of the pelvic viscera will be possible. Approximately 1,000 c.c. of carbon dioxide is injected. The patient is turned on her abdomen, and the head end of the x-ray table is canted down 15 degrees. The buttocks are elevated by means of the 4 inch thick pad placed under the lower abdomen (Fig. 1). The back is arched so that the central ray can be directed between the coccyx and the symphysis pubis. The exposure factors for an average-sized patient are: small focus, 100 Ma., ½ second, 30 inches distance, 75 KVP, Bucky diaphragm.

Pneumoperitoneum is contraindicated in shock, regardless of cause, poor surgical risks, acute pelvic inflammatory state, and in cases where the pathologic lesions are too large for visualization. In addition, the transuterine route is contraindicated in (a) cervicitis; (b) suspected pregnancy; (c) uterine bleeding; (d) tubal obstruction; and (e) intact hymen.

Complete Gynecography

When this simple method of pneumoperitoneum has been mastered and good films obtained, a more refined method of complete gynecography can be used in selected cases. Complete gynecography[12] is pneumoperitoneum plus the injection of iodized oil, and is commonly used for infertility studies. The patient is placed in lithotomy position. The cervix is visualized by means of a speculum, and a self-retaining patency cannula is inserted. We employ a special Graves speculum which is so constructed that it can be disassembled and removed without disturbing the uterine cannula. Before injecting iodized oil, transabdominal pneumoperitoneum is done as previously described. The patient is placed in modified knee-chest position, and the first x-ray film taken. Iodized oil, approximately 4 c.c., is then injected slowly through the previously placed intrauterine cannula, and a second film taken. The position of the patient and the exposure factors remain the same as in the simple pneumoperitoneum described above. A 24 hour control film of the lower abdomen can be taken to establish patency of the tubes as in hysterosalpingography.

The following illustrated case histories demonstrate the value of this simple and accurate method of pelvic diagnosis.

CASE 1.—Mrs. D. P., aged 20 years, gravida 0, married one year, had always had irregular menses, with periods of amenorrhea lasting as long as six months. This patient was chiefly interested in regulating the menstrual cycle. Physical examination was essentially negative. Pelvic examination disclosed a small, anteflexed uterus; the left ovary was the size of a plum; the right ovary was normal to palpation. Transabdominal pneumoperitoneum showed bilateral polycystic ovaries with uterine hypoplasia (Fig. 2). Uterosalpingography was normal. Inasmuch as this patient was not interested in improving her fertility, ovarian resection was not advised at this time.

CASE 2.—Mrs. A. D., aged 22 years, gravida 0, had been married three years. No birth control had been used during the past year. When she was first seen, menses were irregular, occurring at intervals of anywhere from three months to one year. Physical examination was negative. On pelvic examination, the uterus appeared to be smaller than

normal and the adnexa were negative. Complete gynecography in 1948 showed a hypoplastic uterus and bilateral ovarian enlargement (Fig. 3). The ovaries had the appearance of bilateral polycystic ovaries. A semen analysis was normal. Operation was delayed for two years during which time the periods became more irregular. The patient was

Fig. 2.—Bilateral polycystic ovaries.

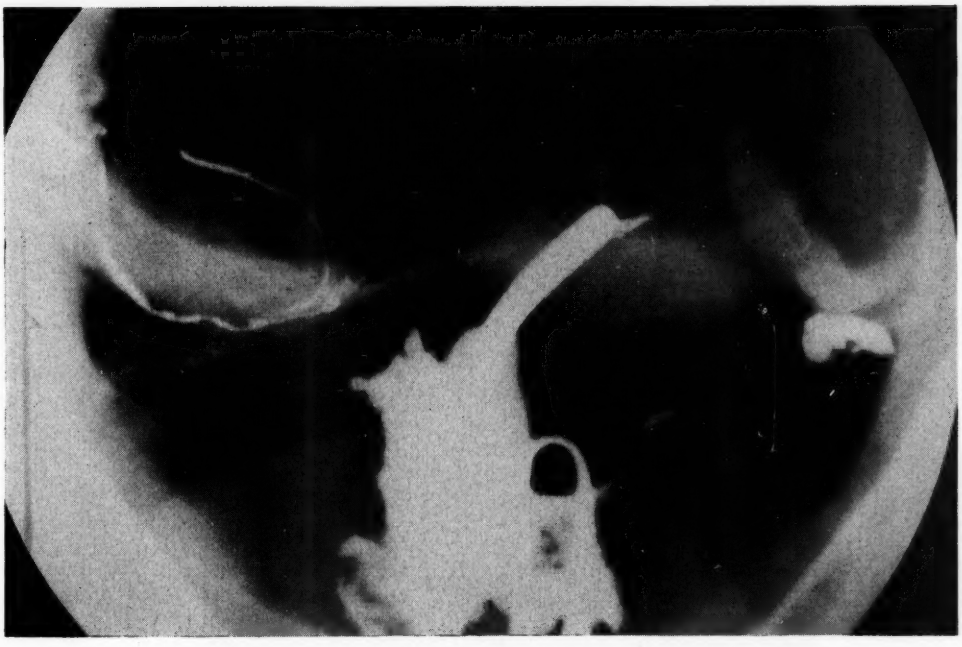

Fig. 3.—Bilateral polycystic ovaries.

Fig. 4.—Transuterine pneumoperitoneum. Right ovarian cyst; small myoma. X-ray and drawing.

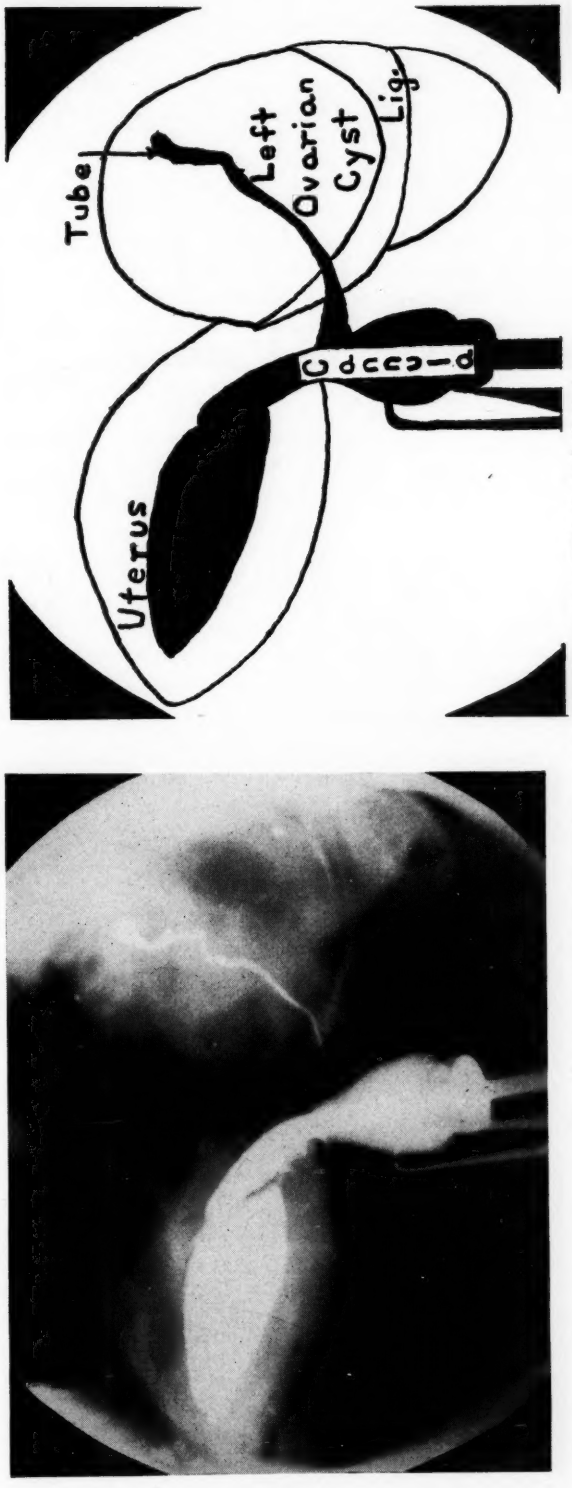

Fig. 5.—Complete gynecography. Left ovarian cyst. X-ray and drawing.

Fig. 6.—Transuterine pneumoperitoneum. Uterine retroversion; moderate hypoplasia. X-ray and drawing.

amenorrheic for one year prior to the time of operation which was performed on July 3, 1950. Bilateral ovarian resection was done for typical bilateral polycystic ovaries. The pathology sections revealed dense compact stroma, numerous large and small follicular cysts, granulosa lined. Following operation, the patient had four menstrual periods at four- to six-week intervals and then conceived. She delivered at full term. Menses have been regular and normal for the past year and one-half.

CASE 3.—Mrs. R. K., aged 19 years, gravida 0, married one year, complained chiefly of infertility of one year's duration. Menses occurred every 14 to 28 days, moderate in amount and of four days' duration. The past history disclosed a left salpingo-oophorectomy at the age of 16, for a twisted dermoid cyst. General physical examination was negative. On pelvic examination, the uterus was normal in size but anteflexed and a mass the size of a small orange could be palpated in the right adnexal region. Transuterine pneumoperitoneum was performed for confirmation of this finding and for tubal patency. Pneumoperitoneum demonstrated an ovarian mass and, in addition, a small subserous myoma was visualized (Fig. 4). At laparotomy, a wedge resection was performed for a hemorrhagic follicular cyst. Oil patency test performed five months after surgery was negative. Repeat iodized oil examination six months later demonstrated patency of the remaining tube. Six months later, the patient conceived and delivered a normal infant at term.

CASE 4.—Mrs. C. M., aged 31 years, gravida 0, complained of infertility. She had been married twice in a four-year period and her past history revealed a right salpingo-oophorectomy which had been performed ten years previously. The physical examination was negative. On pelvic examination the uterus appeared to be normal in size and anteflexed. There was a poorly defined mass in the left adnexal region. Complete gynecography showed a left ovarian mass (Fig. 5). Iodized oil demonstrated patency of the left tube. A semen analysis was normal. No operation was performed and there has been no further follow-up on this patient.

CASE 5.—Mrs. O. V. E., aged 34 years, gravida 0, had been married thirteen years. The patient complained of amenorrhea of twelve years' duration associated with infertility. Physical examination was negative. Pelvic examination showed an extremely small uterus; the adnexa could not be palpated. Pneumoperitoneum confirmed the size of the uterus and outlined very small ovaries (Fig. 6). Therapy was ineffectual.

Comment

The value of gynecography as a diagnostic aid has been well documented in the numerous papers presented by Stein and his associates. Previously this examination has been limited to large institutions because of the need for special equipment. We have demonstrated that excellent films can be taken with the standard x-ray equipment available to every physician. Along with others, we have advocated the injection of gas by the transabdominal route rather than the transtubal route since the former is a more rapid method, producing less discomfort to the patient. Unless sufficient gas (approximately 1,000 c.c.) is injected into the free peritoneal cavity, no visualization of the intrapelvic viscera will be obtained. Little experience is required to obtain good diagnostic films. The interpretation of these films is not difficult, but it does require a knowledge of the normal female internal genitals so that variations in size, shape, and position of adnexal masses can be correctly evaluated. Since these roentgenograms are not distant films, some distortion in size may occur, especially if the patient is obese. It is always possible, how-

ever, to compare the size of each ovary with the size of the uterus. For example, each ovary is normally about one-fourth the size of the uterus; in the Stein-Leventhal syndrome of bilateral polycystic ovaries, each ovary is from one-half to three-fourths the size of the uterus.

Hysterosalpingography is of distinct value in infertility, habitual abortion, and uterine bleeding. When hysterosalpingography is added to pneumoperitoneum, there is additional information available for complete gynecological diagnosis. Moreover, when the use of iodized oil is contraindicated, it is still safe to employ transabdominal pneumoperitoneum for visualization of the uterus and ovaries, and many times distinct tubal outlines are clearly demonstrated. We especially urge all those who are interested in the study of infertility to add gynecography to their diagnostic armamentarium.

Conclusions

1. A simplified method of gynecography utilizing standard x-ray equipment is presented.

2. This method of visualization of the internal genitals by means of pneumoperitoneum with or without iodized oil can be mastered easily.

3. The technique is simple and safe, and diagnostically of the greatest importance since it reveals otherwise obscure pelvic abnormality. It may be performed easily in any hospital or in any x-ray laboratory where standard x-ray equipment is available.

Grateful acknowledgment is made to Dr. Erwin Klein, head of the Radiology Department of Franklin Boulevard Community Hospital, and to his assistant, Miss Trokey, for their aid in developing the roentgenological technique for gynecography with standard x-ray equipment.

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Discussion

DR. IRVING F. STEIN, Sr.—The authors have presented a modification of the technique of gynecography which should encourage more general employment of this valuable aid to gynecologic diagnosis. As in other fields of medicine, x-rays often provide positive evidence of the condition of internal structures, and you have just seen a demonstration of their application to gynecology. No one can doubt the value of such splendid films for differential diagnosis or for obtaining a complete pelvic survey in cases of sterility.

Credit belongs to Peterson and Von Zualenberg for having developed and described the modified knee-chest posture for obtaining x-ray films of the pelvic organs with the use of pneumoperitoneum. In 1921, they reported excellent results with the use of a tilted

table. The procedure proved most awkward, however; it was difficult to keep the patient from sliding off the table and to hold the film cassette under the patient's abdomen. After using their method in 1922, Dr. Arens and I constructed a table which could remain flat and its end leaf, which contained shoulder braces, could lower the patient's head and shoulders to the desired level. The object was to suspend the pelvic organs so that they would be surrounded by carbon dioxide, and the intestines would be displaced from the pelvis. Also, with this arrangement, the pelvis is close to the Bucky diaphragm, thus minimizing distortion. We obtained excellent films, but the table was not available commercially. Recently we modified the Sisk urologic table, employing the same principle; this table is now obtainable for both gynecologic and urologic x-ray studies.

As stated by the essayists, special tables are expensive, and are not always available, especially in small hospitals, laboratories, and physicians' offices. The authors have demonstrated how good diagnostic films can be obtained with the use of the ordinary radiographic table. I wish to emphasize that it is important to have the films as near as possible to the patient's pelvis if one is to avoid distortion and misinterpretation of the findings.

There are many conditions which cannot be diagnosed by the routine methods of examination. In addition to the abnormal conditions mentioned, the demonstration of normal pelvic organs has often been the means of avoiding unnecessary laparotomy. In some cases of undetermined sex, and in the absence of pelvic organs, gynecography has supplied the necessary evidence for diagnosis.

The carbon dioxide may be introduced in three ways, according to applicability in different patients: (1) transuterine insufflation, especially in sterility studies; this route may also be selected for many married women; (2) transabdominal puncture in single girls, children, and as an optional alternative in married women when tubal patency is not an issue; (3) cul-de-sac puncture, with the patient in knee-chest posture, as one would do in culdoscopy.

Usually 1,000 to 1,500 c.c. of carbon dioxide is used in adults and from 300 to 500 c.c. in infants and children.

The authors are to be commended for demonstrating the value of gynecography and for introducing a practical modification of the technique.

DR. COHEN (Closing).—The procedure is in competition with two other procedures, examination under anesthesia and culdoscopy. I wish to stress one point Dr. Stein has already mentioned; that is, gynecography in children. Some pediatricians in Chicago have become very much interested because in many cases it is difficult to tell what the sex of the child is, particularly where the child has mixed male and female organs, with undeveloped genitals and/or hypospadias. In one 3-month-old child on whom gynecography was performed, we very clearly demonstrated an infantile uterus and ovaries. By this method we were able to determine that the child was a female.

TOO MANY "TALENTED" PROSPECTS BY-PASS OBSTETRICS AND GYNECOLOGY

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IN 1953, the American Gynecological Society appointed Howard C. Taylor, Jr. (Chairman), Daniel A. Morton, and the writer, as a Committee to ascertain *why Obstetrics and Gynecology fails to attract its share of "talented" recent graduates!* None of us had the slightest doubt that most brilliant medical students choose other specialties, even though we did not have factual evidence to prove that our specialty was being by-passed by the better young prospects. Hence, at the very outset of our deliberations, we recognized an obligation to determine *whether* Obstetrics and Gynecology has failed to recruit its share of "talented" young physicians. So each of us volunteered to survey the situation in his own medical school, according to his own devices, in a search for evidence which would either prove or disprove the disconcerting premise which led to the appointment of this Committee.

The purpose of this presentation is to report those phases of a detailed survey of Northwestern graduates which are of especial concern to obstetricians and gynecologists. Evidence will be presented which proves the thesis that, at least at Northwestern, our specialty has not attracted its proportionate share of "talented" recent graduates.

In planning this first phase of our investigations, we realized that "talented," whether applied to medical students or recent graduates, is extremely difficult to define and equally hazardous to assess. It was also appreciated that evaluation of a physician's future capabilities, on the basis of his class standing as a medical student, constitutes a highly controversial method of attempting such an appraisal; in fact, some consider this mode of assessing talent as inexcusable effrontery. Nevertheless, even those most resistant to such deductions from grades should concede that prospects with the higher scholastic ratings as students are more likely to become outstanding physicians later. Furthermore, such class standing is actually the only practical and readily available yardstick for classifying recent graduates in respect to their potentialities for future professional achievements. One such tangible future achievement is specialty board certification, an attainment which appealed to us as evidence that a young physician not only possesses talent, but also has demonstrated the ability to use it. Data will be presented to show that such certification has been achieved most frequently by those Northwestern graduates with the highest class standing. Its value as a measure of talent therefore seems valid.

The graduates of Northwestern University Medical School from 1934-1943, inclusive, were selected for this study. A span of ten years was considered necessary, if the sample of graduates was to be sufficiently large so that differ-

ences between groups of them might be statistically significant. Actually 1,613 received the M.D. degree in this particular decade; 68 are deceased, and 1,545 are now listed as active. Furthermore, an interval of fifteen years plus or minus five years has elapsed since the graduation of these classes, and it was assumed that these are the years in which those who will attain specialty board certification are most likely to be so certified. In selecting the graduates of these particular years (1934-1943) for this survey, however, I failed to appreciate how markedly the incidence of specialty board certification had been affected, first, by the rapidly growing popularity of such certification in the 1930's and, later, by the interference, resulting from military service, in the usual time schedule for formal residency training, especially for those graduating in the early 1940's.

The class standing and actual grade achievement at the end of his third year, for each Northwestern graduate, are on file in the office of the Registrar of the Medical School. I am indebted to Dean Richard H. Young for placing these records at my disposal.

The present activities of these graduates were determined from their listings in the 1950 Edition of the American Medical Directory and/or from the 1953 Edition of the Directory of Medical Specialists.

A portion of this survey of recent graduates from Northwestern University Medical School has already been submitted for publication in that school's official journal, *The Quarterly Bulletin.* Certain data from that report will of necessity be included here.

Of the physicians who graduated from Northwestern in the decade 1934-1943, 626, or 40.5 per cent, have already attained specialty board certification. These include 99, or 64 per cent, of the graduates ranking in the first 10 per cent of these classes; 289, or 56 per cent, in the first third; 219, or 42.5 per cent, in the middle third; and 118, or 23 per cent, of those in the last third of these classes.

Data were also presented in that earlier report regarding the various specialties in which these 626 have been certified; they were further classified according to their class standing as medical students. That information is detailed in Table I.

TABLE I. NORTHWESTERN GRADUATES, 1934-1943

SPECIALTY BOARD	CERTIFIED SPECIALISTS		NUMBER CERTIFIED IN EACH CATEGORY OF CLASS STANDING			
	NUMBER	%	NO. IN FIRST 10%	NO. IN FIRST THIRD	NO. IN MID-THIRD	NO. IN LAST THIRD
Internal Medicine*	146	23.3	33	82	44	20
General Surgery†	137	21.9	30	71	46	20
Orthopedic Surgery	61	9.7	5	23	21	17
Obstetrics-Gynecology	55	8.8	4	19	25	11
Ophthalmology	40	6.4	3	12	18	10
Radiology	38	6.1	4	11	16	11
Psychiatry-Neurology	36	5.7	9	19	10	7
Urology	25	4.0	3	11	7	7
Pediatrics	24	3.8	1	8	13	3
Pathology	24	3.8	4	13	7	4
Otolaryngology	22	3.5	2	13	5	4
Dermatology-Syphilis	13	2.1	0	5	6	2
Anesthesiology	4	0.7	1	2	1	1
Physical Medicine	1	0.2	0	0	0	1
Total	626	100	99	289	219	118
Percentage of total number certified			16	46	35	19

Note.—Sixteen per cent of those with specialty board certification ranked in the first 10 per cent of their classes; 46 per cent in the first third; 35 per cent in the middle third; and 19 per cent ranked in the last third.

*Includes 2 certified in Public Health and 6 in Preventive Medicine.

†Includes 6 certified in Plastic, 4 in Thoracic, and 6 in Neurosurgery.

Probably there is nothing more disconcerting to obstetricians and gynecologists in Table I than the evidence that a larger percentage of Northwestern graduates was certified in Orthopedic Surgery than in Obstetrics and Gynecology. It is my considered opinion that Medicine, Surgery, and Obstetrics with Gynecology rank as No. 1, No. 2, and No. 3, respectively, in the major fields of clinical practice. So it was anticipated that Medicine (23.3 per cent) would rank first in the number certified, and that Surgery (21.9 per cent) would be second; accordingly one would expect Obstetrics and Gynecology (8.8 per cent) to rank third. However, it was fourth, and below Orthopedic Surgery (9.7 per cent). This particular fact is not necessarily of great significance since the primary objective of this survey was to determine the quality, not the number of men certified in our specialty.

Next it seemed desirable, if possible, to determine whether the findings recorded in Table I are indicative of a unique situation at Northwestern, or are similar to those which prevail in other medical schools. There is opportunity for some such comparison through certain data found in "Trends in Medical Practice" by H. G. Weiskotten and Marion E. Altenderfer which appeared in *the Journal of Medical Education,* vol. 27, September, 1952, part 2, No. 5, page 3. This is a report on the activities of those who graduated in 1935 and 1940 from all medical colleges in the United States and Canada. Their data were obtained subjectively, i.e., from questionnaires returned by individual graduates. They received replies from only 64 per cent of the 1935 graduates, and from only 70 per cent of those graduating in 1940. In addition they made an effort to obtain information about those who did not reply; in part this was obtained from the 1950 American Medical Directory. As a result *they believed and presented evidence that their questionnaire-obtained data were representative of all graduates from all schools in 1935 and 1940.*

Table II is a comparison of the specialty board certification of Northwestern graduates in 1935 and in 1940 with the certification of those who returned questionnaires of all graduates from all medical schools of the United States and Canada in 1935 and in 1940 (as reported by Weiskotten and Altenderfer in their Table 39). Here, too, those certified in Public Health and in Preventive Medicine are included with those in Internal Medicine; also those certified in Plastic, Rectal, Thoracic, and Neurosurgery are included with those in General Surgery.

TABLE II. PERCENTAGE DISTRIBUTION OF SPECIALTY BOARD CERTIFICATION

	ALL MEDICAL COLLEGES			NORTHWESTERN		
	1935	1940	AVERAGE FOR 1935 AND 1940	1935	1940	AVERAGE FOR 1935 AND 1940
PER CENT CERTIFIED*	33.1%	24.7%	28.9%	39%	47.2%	43.1%
Internal Medicine	22.4†	20.8	21.6	28	28	28
General Surgery	13.7	16.3	15	19.3	26.5	22.9
Orthopedic Surgery	4.7	4.9	4.8	5.3	7.4	6.4
Obstetrics-Gynecology	9.1	6.6	7.9	5.3	13.3	9.3
Ophthalmology	5.8	5.8	5.8	8.8	4.4	6.6
Radiology	7.6	9.5	8.6	5.3	1.4	3.4
Psychiatry-Neurology	9.1	7.6	8.4	8.8	5.9	7.4
Urology	3.9	1.0	2.5	8.8	4.4	6.6
Pediatrics	6.3	9.4	7.9	1.7	4.4	3.1
Pathology	2.6	5.2	3.9	5.3	0	2.7
Otolaryngology	7.5	5.3	6.4	3.4	1.4	2.4
Dermatology-Syphilis	2.6	3.3	3.0	0	2.9	1.5
Anesthesiology	2.2	3.1	2.7	0	0	0
Physical Medicine	0.4	0.3	0.4	0	0	0

*Per cent certified refers (a) for graduates of all medical colleges *to the per cent of the number who returned questionnaires;* it is *not the per cent of the total number* graduated; and (b) for Northwestern, it refers to the per cent of the number now active.

†The percentages recorded for each of the individual specialties refer to the per cent of the total number certified.

Table II shows certain differences between the specialty certification of all graduates, in contrast with that which has occurred among Northwestern Alumni, for example:

1. A larger percentage from Northwestern has attained such certification, both in 1935 (39 per cent vs. 33.1 per cent), and in 1940* (47.2 per cent vs. 24.7 per cent).
2. By comparing the average of the percentages for 1935 and 1940, it is evident that a larger percentage from Northwestern has been certified in Medicine (28 per cent vs. 21.6 per cent), in Surgery (22.9 per cent vs. 15 per cent), in Orthopedic Surgery (6.4 per cent vs. 4.8 per cent), in Obstetrics and Gynecology (9.3 per cent vs. 7.9 per cent), in Ophthalmology (6.6 per cent vs. 5.8 per cent), and in Urology (6.6 per cent vs. 2.5 per cent).
3. On the other hand, a further comparison of the average of the percentages for 1935 and 1940 shows that the percentage certified of Northwestern graduates is *lower in all other specialties.*
4. Finally, and again based on the average of percentages for 1935 and 1940, Obstetrics and Gynecology was tied for fifth place with Pediatrics in the percentage of total number certified of graduates from all medical colleges (it was behind Medicine, Surgery, Radiology, and Psychiatry-Neurology, respectively); on the other hand, at Northwestern in these two years it was third (behind Medicine and Surgery), whereas in the survey for 1934-1943 at Northwestern our specialty was fourth (see Table I), and followed Medicine, Surgery, and Orthopedic Surgery, respectively.

These comparative data in Table II demonstrate that Northwestern graduates were just as avid for and more successful in attaining specialty board certification than the graduates from all medical colleges in the United States and Canada. They also show that the percentage from Northwestern certified in Obstetrics and Gynecology compares favorably; in reality it is a little higher than the percentage certified in this specialty among graduates from all medical schools. These observations suggest that the facts about Northwestern graduates as revealed by this survey, as well as the deductions therefrom, are probably also representative of the graduates from all medical schools.

Our Committee was appointed to ascertain why Obstetrics and Gynecology fails to attract its proportionate share of "talented" recent graduates. *What is a proportionate share?* Table I shows that 626 of those graduated from Northwestern in the decade 1934-1943, inclusive, are now certified by an American Specialty Board. Of that group (as recorded in the last line of Table I) 99, or *16 per cent, were in the first 10 per cent of their classes* when students; 289, or *46 per cent, in the upper third;* 219, or *35 per cent, in the middle third;* and 118, or *19 per cent were in the last third.* The *foregoing percentages are the proportionate share,* of the total, i.e., they represent the average or the normal expectancy in each scholastic category. Hence any specialty which attracts its *proportionate share of "talented" graduates* should have recruited 16 per cent who ranked in the first 10 per cent, and 46 per cent of those certified should be from the upper third of these classes.

Table III details for each specialty *the per cent of the total number certified in that specialty who ranked in each of the four scholastic categories,* i.e., in the first 10 per cent, the first third, the middle third, and the last third of these classes. Here one will learn which specialties have attracted their share of "talented" Northwestern graduates.

From the data in Table III it is evident that:

1. Only 7 per cent of those certified in Obstetrics and Gynecology ranked in the first 10 per cent of their classes; whereas more than three times as many

*Highly significant, probably < 0.01 by the chi-square method.

certified in Medicine* (23 per cent) and in Surgery* (22 per cent) were from this category.

2. Only 35 per cent of those certified in Obstetrics and Gynecology ranked in the upper third of their classes. On the other hand, more than half of those in Medicine* (56 per cent) and in Surgery* (52 per cent) were from the first third of these classes.

3. Almost half of those certified in Obstetrics and Gynecology (actually 45 per cent) ranked in the middle third of their classes; whereas only 30 per cent of those in Medicine* and 33 per cent of those in Surgery were from this group.

TABLE III. PERCENTAGE IN EACH SCHOLASTIC CATEGORY OF TOTAL NUMBER CERTIFIED IN EACH SPECIALTY

AMERICAN BOARDS	TOTAL NUMBER CERTIFIED	PERCENTAGE DISTRIBUTION OF THE TOTAL NUMBER CERTIFIED IN EACH SPECIALTY BASED ON SCHOLASTIC STANDING			
		IN FIRST 10%	IN FIRST THIRD	IN MID-THIRD	IN LAST THIRD
Internal Medicine	146	23	56	30	14
General Surgery	137	22	52	33	15
Orthopedic Surgery	61	8	38	34	28
Obstetrics-Gynecology	55	7	35	45	20
Ophthalmology	40	8	30	45	25
Radiology	38	10	29	42	29
Psychiatry-Neurology	36	25	53	28	19
Urology	25	12	44	28	28
Pediatrics	24	4	33	54	13
Pathology	24	17	54	29	17
Otolaryngology	22	9	59	23	18
Dermatology-Syphilis	13	0	38	46	16
Anesthesiology	4	25	50	25	25
Physical Medicine	1	0	0	0	100
Total number certified	626				
Percentage distribution of the total		16	46	35	19

Note.—Those *percentages in the first 10 per cent* and in the *first third of the class* which are either *average or above normal expectancy,* have been boxed by black lines to make them more conspicuous; i.e., to demonstrate the particular specialties which have attracted Northwestern's more "talented" recent graduates. Obviously the number certified in all specialties, except Medicine and Surgery, is too small for these data to have material significance.

Further *regarding the proportionate share,* in Table I there is detailed for each specialty, the percentage of the 626 certified Northwestern graduates who have been certified in that specialty. Hence for a specialty to attract its proportionate share of "talented" graduates, it should attract the same percentage from those in the first 10 per cent and in the first third of these classes, as it does from the total number certified. For example, 8.8 per cent of the certified Northwestern graduates, in 1934 through 1943, have been certified by the American Board of Obstetrics and Gynecology; hence that specialty's *proportionate share of "talented" graduates* is 8.8 per cent of those in the first 10 per cent of these classes who are certified, and 8.8 per cent of those in the first third of these classes who are certified.

Table IV records for each specialty, the percentage of the total number certified in each scholastic category (i.e., in the first 10 per cent, the first third, etc.) which has been certified in that specialty. Again, but from another aspect, one learns which specialties have attracted their proportionate share of "talented" Northwestern graduates.

*Statistically significant at 5 per cent level by chi-square method.

TABLE IV. PERCENTAGE IN EACH SPECIALTY OF TOTAL NUMBER CERTIFIED IN EACH SCHOLASTIC CATEGORY

AMERICAN BOARDS	PER CENT OF TOTAL NUMBER CERTIFIED	PER CENT OF TOTAL NUMBER THAT HAVE BEEN CERTIFIED IN EACH SCHOLASTIC CATEGORY			
		FIRST 10%	FIRST THIRD	MID-THIRD	LAST THIRD
Internal Medicine	23.3	33.3	28.3	20	16.9
General Surgery	21.9	30.2	24.5	21	16.9
Orthopedic Surgery	9.7	5.1	7.9	9.6	14.4
Obstetrics-Gynecology	8.8	4.1	6.6	11.5	9.4
Ophthalmology	6.4	3.0	4.4	8.2	8.5
Radiology	6.1	4.1	3.8	7.3	9.4
Psychiatry-Neurology	5.7	9.1	6.6	4.6	5.9
Urology	4.0	3.0	3.8	3.2	5.9
Pediatrics	3.8	1.0	2.7	5.9	2.6
Pathology	3.8	4.1	4.5	3.2	3.3
Otolaryngology	3.5	2.0	4.5	2.3	3.3
Dermatology-Syphilis	2.1	0	1.7	2.7	1.7
Anesthesiology	0.7	1.0	0.7	0.5	0.9
Physical Medicine	0.2	0	0	0	0.9
Number certified	626	99	289	219	118

Note.—Those *percentages in the first 10 per cent* and in the *first third of the classes* which either *equal or surpass the proportionate*, i.e., the recorded per cent of the total number who have been certified in that specialty, again have been boxed by black lines to make them more conspicuous, i.e., to demonstrate, once more, the particular specialties which have attracted their proportionate share, or more, of Northwestern's "talented" graduates. Of course they are the same specialties which one finds so designated in Table III. Again the total number certified in most specialties is so small that these data may not have material significance.

The data in Table IV show the following, and it is disconcerting to Obstetricians and Gynecologists:

1. Although 55.4 per cent of Northwestern's graduates certified by specialty boards are certified in Medicine, Surgery, Psychiatry-Neurology, Pathology, and Anesthesiology, these five specialties attracted 77.7 per cent of those in the first 10 per cent of these classes who are certified, i.e., 40 per cent *more than their proportionate share* from this elite group; they also attracted 64.6 per cent of those certified in the first third of these classes, or 16.6 per cent *more than their proportionate share* from the group of better than average students.

2. On the other hand, 8.8 per cent of the certified group at Northwestern are certified in Obstetrics and Gynecology, but that specialty attracted only 4.1 per cent of those certified in the first 10 per cent of these classes, i.e., *54 per cent less than its proportionate share of the top-flight students;* furthermore, it attracted only 6.6 per cent of those certified in the first third of these classes, or *25 per cent less than its share of the better students.* (The number certified in Obstetrics and Gynecology may be too small for these data to have material significance.)

3. It is probably significant, however, that Medicine and Surgery together accounted for 45.2 per cent of the total number certified, but that included 63.5 per cent of those certified in the first 10 per cent of these classes, or 40 per cent *more* than their proportionate share; they further accounted for 52.8 per cent of those in the first third of these classes, or 17 per cent *more* than their share of the better students.

4. In consequence most specialties have suffered, and about equally, because of this domination of talent by Medicine and Surgery. Such monoply of the better prospects has been calamitous not only for Obstetrics and Gynecology

but also for Orthopedic Surgery, Ophthalmology, Radiology, Urology, Pediatrics, Otolaryngology, and Dermatology-Syphilis. Actually these eight specialties have accounted for 44.4 per cent of the total number certified, yet they can lay claim to only 22.3 per cent of those certified in the first 10 per cent of these classes, i.e., 50 per cent *less* than their proportionate share. Further they accounted for only 35.4 per cent of those certified in the first third of these classes, or 20 per cent *less* than their share of the better students.

5. The specialty of Obstetrics and Gynecology ranked fourth in the percentage of the total number certified (behind Medicine, Surgery, and Orthopedic Surgery), but it was eleventh in the percentage of those who had been in the first 10 per cent of their classes; it was tenth, in the first third; it tied for third place, in the middle third; and it ranked sixth in the percentage who had been in the last third of their classes.

Hence in this particular survey *the specialty of Obstetrics and Gynecology appears to have specialized in mediocrity; it failed to attract the "talented" graduates.*

Comment

This survey of the 1934-1943 graduates from Northwestern University Medical School has produced evidence proving that Obstetrics and Gynecology fails to attract its proportionate share of the more "talented" young physicians. At least that is the situation at Northwestern. On the other hand, a comparative study of certain data about Northwestern's recent graduates with the "Trends in Medical Practice" manifested by graduates from all medical schools (see Table II) suggests that this same humiliating state of affairs probably exists among all recent graduates, and that it is not unique for Northwestern. In fact, I am fairly certain that the findings at Northwestern are not isolated phenomena, but are representative, and it seems probable that all but the most complacent of readers will have similar suspicions. Nevertheless, when "applications for residencies by talented students" was used as the basis for opinion, and this proposition was included in a questionnaire which our Committee submitted to 84 chairmen of departments of Obstetrics and/or Gynecology in the United States, 75, or 89 per cent, replied; but only 30 of these chairmen, or 40 per cent, believed that our specialty now fails to receive its share of "talented" medical students.

Hence its is anticipated that others will make similar surveys of their graduates; in fact it appears almost mandatory that this be done by some of that 60 per cent who by their answers to the questionnaire disagree with the proposition which our Committee was asked to investigate. If at only one school or a few schools the more "talented" graduates by-pass our specialty, then the causes for our lack of popularity and failure to appeal must be local; they will be discovered within the limitations of the faculty and the four walls of those particular schools. On the other hand, if the data from Northwestern are fairly representative of the situation in all schools, or in most schools, then the major causes are general; in fact they are fundamental and deep seated. By the same token, corrective measures must be on a general level where they can influence the entire specialty, rather than on a local plane and aimed at correcting conditions in a few institutions.

THE EFFECT OF NORMAL AND TOXEMIC PREGNANCY ON BLOOD PRESSURE

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CLINICAL studies originated in Sloane Hospital for Women in 1927, 1934, and 1936 which stressed the association of toxemia of pregnancy and cardiovascular renal disease. These studies indicated that toxemia of pregnancy was not always an isolated state, for either hypertensive vascular disease or Bright's disease was present in many patients following delivery. Such conclusions resulted from long follow-up studies and correlation of autopsy findings in 11 patients who had experienced toxemia of pregnancy. The interrelationship of toxemia of pregnancy and cardiovascular renal disease was emphasized in one study which indicated that the majority of the deaths which occurred in women who had had toxemia of pregnancy were from causes within the cardiovascular renal field.

These were observations made approximately twenty years ago. Since then numerous similar investigations have become available and the importance of hypertensive vascular disease in obstetrics is well established. Despite the many painstaking, meticulous observations, however, the enigma of the relationship remains. There is still no unanimity of opinion regarding the answer to these fundamental questions: (1) does toxemia of pregnancy incite hypertension, (2) does toxemia of pregnancy aggravate hypertensive disease when it is present, (3) does toxemia of pregnancy arise in the individual destined to develop hypertension?

It became evident about 1937 when Reid and Teel presented evidence, corroborated by Browne, Chesley, and me, of the frequent decrease in the levels of hypertension in the mid-trimester of pregnancy, that studies based on the behavior of blood pressure levels during pregnancy could be subject to wide error. The assumption inherent in previous studies that normal blood pressure values in early pregnancy implied normotension required re-evaluation, as it was plainly evident that, if severely hypertensive values could decrease, lesser values might also abate and enter the apparently normal range. Such behavior of blood pressure makes it apparent that studies initiated in pregnancy could not determine the instigating or aggravating affect of toxemia of pregnancy. To determine this, knowledge of blood pressure readings prior to every studied pregnancy would be required.

While previous studies with which I was associated included many patients with documented prepregnancy blood pressures, the majority were first observed early in pregnancy. It was therefore determined to re-examine the relationship of hypertension to toxemia of pregnancy, using only those patients whose blood

pressures were documented prior to a closely observed first pregnancy, and in whom follow-up data were available. First pregnancy observations were employed so as to avoid: (1) the possible influence of the unobserved pregnancy, (2) the extraneous causes of hypertension which could arise in the interim between pregnancies, and (3) the possible age factor. In this way, the variables of pregnancy, toxemia, and hypertension could be kept to a minimum, and the relationship among them more clearly defined.

The collection of cases began approximately in 1937, at first haphazardly, and later more energetically (1942 to 1945 excluded). Data have been slowly accumulated. Review of untold numbers of hospital charts, files of toxemia patients, and repeated query of current clinic and private patients furnished the material for this study. Private physicians, hospitals, schools, universities, and business organizations were contacted for possible blood pressure records prior to pregnancy. All available blood pressure readings were solicited. In order to secure as many cases as possible, no time limit between blood pressure and first pregnancy was adopted. Nevertheless, in this relatively long period of time, by individual effort, less than 500 cases became available for study, many of which eventually could not be used, because on re-examination, the criteria demanded were not fullfilled. It must be borne in mind that, while this was a selected group in one sense, the selection depended on the chance presence of documented blood pressure value preceding a first pregnancy.

Since this report deals principally with blood pressure values, it is necessary to describe the characteristics of these determinations which can cause difficulties in their measurements. Only in this way can the conclusions drawn from such data be fully evaluated. These qualities peculiar to blood pressure include: (1) lability, in both normal and abnormal range, (2) association of temporary elevation with future sustained elevation, (3) immediate response by elevation to many stimuli, (4) lack of universal definition of the lower pathologic limits.

Long clinical experience suggests that in some individuals transient rises of blood pressure introduce more sustained and severe hypertension. Such observations have been made by von Monakow, Stieglitz, and the late W. W. Herrick. Clinical studies have substantiated such opinions. Diehl and Hesdorffer studied 155 young men at the University of Minnesota 5 to 10 years, an average interval of 7 years, after the original blood pressure readings, and reached the conclusion that young men who show elevations of blood pressure, even though these are transient, are more likely to have high blood pressure after 5 to 10 years than those whose blood pressure was constantly within normal limits. The normal group consisted of those whose blood pressure was always under 130 mm. Hg. The transient group consisted of those who gave only one reading above 130 mm. Hg. Constant, intermittent, or transient rises of blood pressure between 130 and 140 mm. Hg. indicated a tendency to elevated blood pressure. Hines, at the Mayo Clinic, reviewed the records of 1,522 patients, 10 and 20 years after the initial blood pressure reading. He associated the transient increase of blood pressure at the first visit with the cold pressor test, and called it a psychic pressor test. He stated that excessive variability or excessive response of the usually normal blood pressure to stimulation should

be considered evidence of a possible prehypertensive state. His table indicates that with initial systolic readings of 130-139 mm. Hg, 10 per cent of patients show hypertension (160/100) 10 years later, and 33.8 per cent 20 years later; with 140-149 mm. Hg as an initial reading, 39 per cent show hypertensive disease 10 years later, and 63.1 per cent 20 years later. Patients with diastolic blood pressures from 85-89 mm. Hg showed hypertension in 25 per cent of the cases 10 years later, and in 57.3 per cent 20 years later. He also stated that if blood pressure does not rise above 120/70 mm. Hg, the patient is almost certain not to have hypertension later.

Master, in a follow-up study of 50 patients, all over 40 years of age, who had had one blood pressure reading between 140 and 156 mm. Hg systolic, and 80 and 94 mm. Hg diastolic while hospitalized 1 to 7 years previously, found that 38 of the 50 patients had hypertension; at least 25 per cent had diastolic readings over 100 mm. Hg. In his view, even one single borderline blood pressure reading might have significance. Hillman, Levy, Stroud, and White analyzed the records of 22,741 officers of the U. S. Army with transient hypertension, using 150/90 mm. Hg as a standard of hypertension. Eighty-four per cent of the men were under observation from 5 to 19 years. They concluded that at all ages sustained hypertension developed more frequently in those with previous transient hypertension than in those who never showed an elevation of blood pressure. Browne, in 1947, stated that the blood pressure of the pregnant woman does not rise significantly with nervousness; if it does, she is hypertensive, or potentially so. He also pointed out that the first blood pressure reading, if elevated, in pregnancy, is the early warning, and showed that the blood pressure becomes permanently elevated in 65 per cent of these women later in pregnancy.

The blood pressure readings in this study were secured wherever available. This implies casual reading by many different individuals, under ambulatory and hospital conditions, occasionally in the presence of febrile or convalescent states. These are factors which materially affect levels of blood pressure and undoubtedly contribute to the lack of smoothness of the data. Criticism may be leveled at this report because such readings may be considered inaccurate, but it was the only way possible for the accomplishment of this study. It should be recalled that while many techniques for the determination of blood pressure have been devised by different investigators, so that consistent readings may result, under controlled conditions, Ayman and Goldshine who checked blood pressure readings taken at home and at the clinic in 34 hypertensive patients concluded, "It is our experience that a patient with essential hypertension can no more become non-reactive to the physician by repeated visits than he can become non-reactive to the pressor test of cold or breath holding."

The determination of blood pressure is relatively simple, and its technique has been widely taught for over 40 years. Casual readings more accurately reflect daily variations than the so-called basal readings. It is well known that psychic and emotional stimuli produce elevations of blood pressure. Many studies have demonstrated such effect. Zabel believed that at least 50 blood

pressure determinations were required to eliminate the rise in blood pressure due to emotional stress. The impact of emotion on blood pressure is so well recognized that it is common practice for many physicians when taking blood pressure or confronted with readings above 130-140/95 to take several readings, chart the lowest and attribute the highest levels to the emotional excitement of the examination. Very likely some of the records used in this paper have been affected by such reasoning.

Granted that functional stress can produce nonsustained rises of blood pressure, the studies of Mueller and Brown in 26 normal and 61 hypertensive subjects who were hospitalized indicate that rhythmic changes in blood pressure took place throughout the day and night. Hourly readings showed systolic variations of 15 to 65 mm. Hg in the normal, and 25 to 120 mm. Hg in the hypertensive. The diastolic pressure also varied to a lesser degree. Kilpatrick, in 1948, confirmed these conclusions after a detailed study by indicating that casual readings in a patient with essential hypertension are exceedingly variable.

There is little difficulty in the determination of hypertension when the blood pressure level is high. There is no general agreement, however, on the lower limits of hypertension. This value must exist, variable and nebulous as it may be, for the earliest sign and first objective finding of hypertensive vascular disease is the rise of blood pressure. In its absence, the asymptomatic and insidious onset of hypertensive vascular disease cannot be recognized.

The standards employed by obstetricians and internists vary. Browne used 130/70 mm. Hg up until 1940, since then 120/80 mm. Hg. Eastman employs 140/90 mm. Hg, but is concerned about a level of 135/85 mm. Hg. Dieckmann also states in his text that 140/95 mm. Hg, or more, on several days is abnormal, but in determining blood pressure for normal pregnancy excluded patients with systolic blood pressure of 130 mm. Hg or higher on two or more occasion. All these figures are pertinent to pregnancy. Similarly, the internist employs 140/90, 150/90-95, 150/100, and 160/100 mm. Hg for levels of abnormal blood pressure. Robinson and Brucer concluded, from a study of 7,478 men and 3,405 women, that systolic blood pressure ranges from 90 to 120 mm. Hg and the diastolic blood pressure ranges from 60 to 80 mm. Hg. They dealt with life insurance material which considers levels beyond which there is increase of mortality. More recently, Master, Garfield, and Walters use 140/90 to 165/100 mm. Hg for the woman from 16 to 44 years as the lower limit of hypertension. Bechgaard believes, on the basis of an extensive review of the pertinent literature, that most young people have a systolic blood pressure below 130 mm. Hg, and that most physicians take this view, but do not dare pronounce blood pressure between 130 mm. Hg and 140 mm. Hg as hypertensive.

From what has been said, it is evident that blood pressure readings are not fixed, and while elevated readings can be labile and transient, in many instances they imply future sustained hypertension. This concept becomes most important in the examination of the affinity between toxemia and hypertension, as it introduces the possibility that there is no relationship between the two in the postpartum period.

The series under study includes 240 patients with normal and 137 patients with toxemic pregnancy.

The criteria for a normal pregnancy included an observation period of at least the last four months of pregnancy, labor, and a hospital stay of at least six days, blood pressure readings not in excess of 129 mm. Hg systolic and 89 mm. Hg diastolic (actually, if 3 readings reached 128 mm. Hg systolic or 88 mm. Hg diastolic, the case was excluded), and negative urine (proteinuria, one plus, on one occasion was permitted). Cases with a background of thyroid disease, cardiovascular renal disease, and diabetes were excluded.

The criteria for toxemia as used in this study were as follows:

1. Hypertensive Toxemia.—The appearance of blood pressure values at any time in pregnancy exceeding 130/90 mm. Hg, or more, on at least 3 occasions, 24 hours apart. If blood pressure values conformed to these criteria in the antepartum state, and then were decreased in labor, the case was excluded from the series. Actually, when a value of 130/90 mm. Hg was reached in pregnancy, higher levels invariably followed. Proteinuria, more than 1 plus, on three occasions, edema, other than the most minimal of the ankles, and symptoms of central nervous system origin were cause for exclusion. Several cases, because of the apparent sudden appearance of hypertension late in pregnancy, might be classified "pre-eclampsia" in many clinics.

2. Pre-eclampsia and Eclampsia.—Acute or gradual onset of blood pressure values above 130/90 mm. Hg; proteinuria exceeding 3 plus; significant edema, generalized or involving at least two of the following: feet, hands, face; symptoms of central nervous system involvement; epigastric pain; elevated uric acid; and decrease of serum protein. Not all criteria were required in any one case, but hypertension and proteinuria were basic requirements. Four patients with the criteria just enumerated had convulsions. In cases of pre-eclampsia with antecedent hypertension, edema and 3 to 4 plus proteinuria were required. Any case in which classification was not clear-cut and which did not fulfill the criteria given was excluded.

Nearly all tables in this study were prepared so as to avoid the omission of possibly significant data originating in the variability of blood pressure determination. This meant that the calculations were done in duplicate. Two tables were constructed using both the highest systolic and diastolic values and the lowest systolic and diastolic values available for any patient. Only one determination was used for each patient, regardless of the number at hand. When only one value was present, it was used in both tables. In this way, averages would not mask the implication of transient elevations, and conversely, averages of lower values, unless also elevated, would negate the importance of temporary peaks.

The pre-eclampsia-eclampsia group, clinically indistinguishable at the peak of toxemia, was divided arbitrarily into 2 groups, dependent on blood pressure readings above 129/89 mm. Hg in the prepregnant state.

Table I illustrates that a pregnancy which is normal and which conforms to the standards stated is preceded nearly 90 per cent of the time by blood pressure determinations of below 129/89 mm. Hg, while toxemic pregnancy will show in 60 per cent of cases systolic readings above 129 mm. Hg, and in 40 per cent diastolic readings above 89 mm. Hg. Blood pressures between 130 and 139 mm. Hg were seen three times as commonly before toxemic pregnancy (28.5 per cent) as before normal pregnancy (9.5 per cent).

The level of 130 mm. Hg systolic was employed as the lower limit of abnormal systolic blood pressure because it has been considered prehypertension or early hypertension by some writers, and because such levels may be the first evidence in pregnancy of the onset of a fulminating toxemia.

TABLE I. SUMMARY OF HIGHEST BLOOD PRESSURE VALUES PRECEDING NORMAL AND TOXEMIC PREGNANCIES

MM. HG	NORMAL (240)		TOXEMIA (137)	
	NO.	%	NO.	%
Systolic.—				
129–	210	87.5	53	38.7
129+	30	12.5	84	61.3
130-139	23	9.5	39	28.4
Diastolic.—				
79–	149	62.1	45	32.8
79+	91	37.9	92	67.2
89–	225	93.7	85	62.0
89+	15	6.3	52	38.0

Table II shows the breakdown of systolic and diastolic blood pressures according to the specific clinical form of toxemia which followed these values.

In approximately an equal division of cases, it is clear that all forms of toxemia may be preceded by any level of blood pressure. Systolic measurements below 130 mm. Hg were present in only 17 cases (26 per cent) of hypertensive toxemia, contrasted with 42 cases (59 per cent) of pre-eclampsia and eclampsia. Differences were also apparent in the diastolic reading. Thirteen cases (20 per cent) had values below 79 mm. Hg, compared with 35 cases (49 per cent) of the pre-eclampsia-eclampsia group. At levels above 90 mm. Hg this relationship was reversed; 35 cases (53 per cent) of the hypertensive group were in this range, as opposed to 20 cases (28 per cent) of the pre-eclampsia and eclampsia.

These findings indicate that higher levels of blood pressure were more common before the hypertensive form of toxemia than before pre-eclampsia and eclampsia.

One hundred seventy (45 per cent) of the 377 patients furnished blood pressure observations within one year of the beginning of pregnancy. The remainder of the observations, 200 (55 per cent), was obtained from 1 to 5 years before pregnancy. This comprises a time interval sufficiently long for blood pressure to change. A normal determination made 5 years previously may represent the only observation of an individual who subsequently became hypertensive. Similarly, the blood pressure at a peak from emotion may depict a normotensive individual. Ideally, this study should consist only of blood pressures obtained within 2 to 3 months before the onset of pregnancy.

TABLE II. BLOOD PRESSURE VALUES PRECEDING A FIRST PREGNANCY, ACCORDING TO TYPE OF TOXEMIA

MM. HG	HYPERTENSION	PRE-ECLAMPSIA AND ECLAMPSIA
Systolic.—		
109–	1	3
119–	5	24
129–	11	15
139–	25	13
149–	10	10
159–	6	3
160+	8	3
Diastolic.—		
69–	3	4
79–	10	31
89–	18	16
99–	20	15
109–	9	4
119–	6	–
120+	–	1

TABLE III. MEAN HIGHEST SYSTOLIC AND DIASTOLIC BLOOD PRESSURE VALUES, STANDARD DEVIATION, AND MEAN AGE FOR FIVE YEARS PRECEDING, AND ONE TO FOUR YEARS FOLLOWING, A FIRST NORMAL PREGNANCY (218 PATIENTS)

	PRECEDING PREGNANCY						POST PARTUM
	5 YEARS	4 YEARS	3 YEARS	2 YEARS	1 YEAR	6 MONTHS	1-4 YEARS
No. of cases	24	23	32	49	38	52	93
Age (years)	20.7	20.5	21.6	22.3	24.3	25	27.6
Systolic (mm. Hg)	118.5	120	120	116.8	119.6	116.8	116.7
Standard deviation	9.9*	15.6*	9.2	8.5	11.4	11.2	12.5
Diastolic (mm. Hg)	78.8	78.8	76.7	75.1	76.7	76.1	76.2
Standard deviation	8.4*	10.8*	8.7	7.6	10.3	9.7	10.9

*Corrected.

TABLE IV. MEAN LOWEST SYSTOLIC AND DIASTOLIC BLOOD PRESSURE VALUES, STANDARD DEVIATION, AND MEAN AGE FOR FIVE YEARS PRECEDING, AND ONE TO FOUR YEARS FOLLOWING, A FIRST NORMAL PREGNANCY (218 PATIENTS)

	PRECEDING PREGNANCY						POST PARTUM
	5 YEARS	4 YEARS	3 YEARS	2 YEARS	1 YEAR	6 MONTHS	1-4 YEARS
No. of cases	20	24	34	50	40	50	93
Age (years)	21.4	19.9	22	21.8	24.8	24.8	27.7
Systolic (mm. Hg)	113.4	114.6	114.7	111.0	112.4	112.7	113.6
Standard deviation	11.4	14.1	10.0	11.1	12.6	8.7	12.0
Diastolic (mm. Hg)	72.8	72.8	72.3	69.8	70.5	72.2	73.3
Standard deviation	11.4	6.7	11.4	10.7	9.8	11.1	13.6

Tables III and IV show the number of cases, mean age, highest and lowest calculated mean systolic and diastolic blood pressure and standard deviation of 218 patients preceding and 93 patients following normal pregnancy. The consistency within 3.7 mm. Hg of mean systolic and diastolic blood pressure, the result of 452 chance individual observations is demonstrated over the five-year interval preceding pregnancy. In Table III the mean highest value ranges from 116.8 to 120 mm. Hg systolic and from 75.1 to 78.8 mm. Hg diastolic, and in Table IV the mean lowest value ranges from 111 to 114.7 mm. Hg systolic and from 69.8 to 72.8 mm. Hg diastolic. The maximum spread between the highest and lowest blood pressure determinations (Table III and Table IV) is 9 mm. Hg (111 to 120 mm. Hg systolic and 69.8 to 78.8 mm. Hg diastolic). The standard deviation, an index of the variability of blood pressure, with one exception in both tables, is relatively small and constant and in conjunction with the mean value suggests the presence of a homogeneous vascular pattern among these cases. This group is characterized by a mean blood pressure well within normotensive levels and a range of 86 to 151 mm. Hg systolic and 48 to 100 mm. Hg diastolic (mean plus or minus two times the standard deviation). It is evident that some blood pressure determinations preceding a normal pregnancy may reach accepted hypertensive levels.

Follow-up observations, for from 1 to 4 years, available in 93 patients, indicate no significant change in mean value and standard deviation, regardless of whether the highest or lowest determination was used in its derivation (standard error of difference between means equals 1.9). Following a normal pregnancy the range of the blood pressure is 90 to 142 mm. Hg systolic and 46 to 101 mm. Hg diastolic.

Tables III and IV indicate therefore that blood pressure is not affected by normal pregnancy within 1 to 4 years of its completion and that the great majority of women exhibit casual normal blood pressure levels preceding normal pregnancy.

TABLE V. MEAN HIGHEST SYSTOLIC AND DIASTOLIC BLOOD PRESSURE VALUES, STANDARD DEVIATION, AND MEAN AGE FOR FIVE YEARS PRECEDING AND ONE TO FOUR YEARS FOLLOWING A FIRST PREGNANCY WITH BLOOD PRESSURE LEVELS ABOVE 130/90

	PRECEDING PREGNANCY			POST PARTUM
	5-4 YEARS	3-2 YEARS	1 YEAR –	1-4 YEARS
No. of cases	13	29	24	32
Age (years)	22.6	26.2	27.7	29.5
Systolic (mm. Hg)	134.4	136.6	141	140.9
Standard deviation	19.9*	13*	19.6*	22.5
Diastolic (mm. Hg)	87.5	88.2	92.1	90.8
Standard deviation	11.6*	13.6*	13.4*	13.5

*Corrected.

TABLE VI. MEAN LOWEST SYSTOLIC AND DIASTOLIC BLOOD PRESSURE VALUES, STANDARD DEVIATION, AND MEAN AGE FOR FIVE YEARS PRECEDING AND ONE TO FOUR YEARS FOLLOWING A FIRST PREGNANCY WITH BLOOD PRESSURE LEVELS ABOVE 130/90

	PRECEDING PREGNANCY			POST PARTUM
	5-4 YEARS	3-2 YEARS	1 YEAR –	1-4 YEARS
No. of cases	13	30	23	32
Age (years)	23.0	25.4	28.4	30.5
Systolic (mm. Hg)	124.3	127.6	132.5	131.3
Standard deviation	16.4	11.7	20.5	19.5
Diastolic (mm. Hg)	79.5	79.8	85.0	83.7
Standard deviation	6.7	12.2	15.1	11.2

Tables V to VI present the findings in 66 patients preceding, and 32 patients following, the hypertensive forms of toxemia of pregnancy. These tables, identical in construction with that of normal pregnancy, except for the employment of two-year time intervals, were assembled from 136 available prepregnancy blood pressure determinations.

In contradistinction to the behavior of blood pressure prior to a normal pregnancy, there is a progressive increase of 6.6 and 8.2 mm. Hg in mean systolic and 4.6 and 5.5 mm. Hg in diastolic value with the advance of years. This is a small series numerically, and the significance of this increase of blood pressure paralleling age cannot be determined. The mean highest value ranges from 134.4 to 141 mm. Hg systolic, and from 87.5 to 92.1 mm. Hg diastolic, and the mean lowest value ranges from 124.3 to 132.5 mm. Hg systolic and 79.6 to 85.0 mm. Hg diastolic preceding pregnancy. The maximum spread between the mean highest and lowest systolic blood pressures in the same year is 10.1 mm. Hg and between the diastolic values is 8.4 mm. Hg. But the spread over the five-year interval between mean highest and lowest systolic (Tables V and VI) values is 16.7 mm. Hg (124.3 to 141 mm. Hg) and between the highest and lowest diastolic values is 12.6 mm. Hg (79.5 to 92.1 mm. Hg). The mean lowest systolic blood pressure in the group 5 years before pregnancy exceeded the mean highest systolic value available before normal pregnancy by 4.3 mm. Hg. While this is also true in diastolic value, the difference is insignificant (0.7 mm. Hg). The standard deviation is large and frequently doubles that seen before normal pregnancy. In conjunction with the mean value it indicates that these patients have higher and more variable blood pressure, frequently in the hypertensive range, long before pregnancy.

This slightly older group is characterized by its heterogeneity of blood pressure values with mean values in the suspiciously hypertensive zone within a year before pregnancy (systolic 132.5 to 141 mm. Hg, diastolic 85 to 92.1 mm. Hg). The extent of the range from 92 to 180 mm. Hg systolic and from 55 to 119 mm. Hg diastolic (mean plus or minus 2 standard deviations) is greater than that prior to a normal pregnancy. In the follow-up, the high and low

systolic values differ by 9.6 mm. Hg (140.3 to 131.3 mm. Hg) and the diastolic values by 7.1 mm. Hg. (90.8 to 84 mm. Hg). This is not statistically significant (standard error of the difference between the means equals 1.8, 2.3). As with normal pregnancy, both high and low mean postpartum determinations are nearly identical with those of the prepregnant period.

TABLE VII. MEAN HIGHEST SYSTOLIC AND DIASTOLIC BLOOD PRESSURE VALUES, STANDARD DEVIATION, AND MEAN AGE FOR FIVE YEARS PRECEDING AND ONE TO FOUR YEARS FOLLOWING A FIRST PREGNANCY WITH PRE-ECLAMPSIA (129/89)

	PRECEDING PREGNANCY			POST PARTUM
	5-4 YEARS	3-2 YEARS	1 YEAR –	1-4 YEARS
No. of cases	9	14	18	30
Age (years)	21.2	22.1	26.6	28.5
Systolic (mm. Hg)	110.8	116.4	118.6	121.5
Standard deviation	7*	4.6*	9.4*	12
Diastolic (mm. Hg)	73.6	75	76.1	78.8
Standard deviation	13.2*	6.4*	6*	13.5

*Corrected.

TABLE VIII. MEAN LOWEST SYSTOLIC AND DIASTOLIC BLOOD PRESSURE VALUES, STANDARD DEVIATION, AND MEAN AGE FOR FIVE YEARS PRECEDING, AND ONE TO FOUR YEARS FOLLOWING, A FIRST PREGNANCY WITH PRE-ECLAMPSIA (129/89)

	PRECEDING PREGNANCY			POST PARTUM
	5-4 YEARS	3-2 YEARS	1 YEAR –	1-4 YEARS
No. of cases	13	12	16	30
Age (years)	18.8	22.5	25.9	28.6
Systolic (mm. Hg)	105.4	111.5	114	114.4
Standard deviation	13.3	7.3	10	9.8
Diastolic (mm. Hg)	64.4	72.5	70.1	74.5
Standard deviation	13.3	4.0	9.4	9.8

Tables VII and VIII present the findings in 41 patients preceding and in 30 patients following pre-eclampsia and eclampsia (4 patients). Fifty-two prepregnancy blood pressure determinations were available for study. In this series the increase of mean determination with age is also noticeable. The mean highest value ranges from 110.8 to 118.6 mm. Hg systolic and from 73.6 to 76.1 mm. Hg diastolic and the mean lowest value from 105.4 to 114.0 mm. Hg systolic and 64.4 to 70.1 mm. Hg diastolic. The maximum spread between the mean highest and lowest systolic blood pressure in the same year is 5.4 mm. Hg and between the diastolic values is 9.2 mm. Hg. The spread over the five-year interval between mean highest and lowest systolic (Tables VII and VIII) is 13.2 mm. Hg (105.4 to 118.6 mm. Hg) and between the highest and lowest diastolic values is 11.7 mm. Hg (64.4 to 76.1 mm. Hg). The standard deviation is small and closely approximates that seen before normal pregnancy and is frequently less than half the value encountered before a hypertensive pregnancy. The standard deviation and the mean value again demonstrate a homogeneity of the vascular patterns. This could be predicted as the group was selected so that the blood pressure did not exceed 129/89 mm. Hg before the pregnancy. The prepregnancy behavior of these determinations is identical with that seen before normal pregnancy. Follow-up observations for 1 to 4 years in 30 patients indicate no significant change in mean value and standard deviation, regardless of whether the highest or lowest determination was used in its derivation (standard error of difference between the means equals 0.9). Following an acute toxemia of pregnancy in 30 patients with previously normotensive determinations the range of blood pressure was 95.0 to 146.0 mm. Hg systolic and 52.0 to 106.0 mm. Hg diastolic.

TABLE IX. MEAN HIGHEST SYSTOLIC AND DIASTOLIC BLOOD PRESSURE VALUES, STANDARD DEVIATION, AND MEAN AGE FOR FIVE YEARS PRECEDING, AND ONE TO FOUR YEARS FOLLOWING, A FIRST PREGNANCY WITH PRE-ECLAMPSIA (130/90+)

	PRECEDING PREGNANCY			POST PARTUM
	5-4 YEARS	3-2 YEARS	1 YEAR –	1-4 YEARS
No. of cases	5	9	16	21
Age (years)	22.4	29.2	26.3	29.8
Systolic (mm. Hg)	139.5	140.8	147.8	147
Standard deviation	4.5*	9.9*	28*	25*
Diastolic (mm. Hg)	90.5	91.4	92.2	90.4
Standard deviation	9.1*	6.4*	17*	14.7*

*Corrected.

TABLE X. MEAN LOWEST SYSTOLIC AND DIASTOLIC BLOOD PRESSURE VALUES, STANDARD DEVIATION, AND MEAN AGE FOR FIVE YEARS PRECEDING, AND ONE TO FOUR YEARS FOLLOWING, A FIRST PREGNANCY WITH PRE-ECLAMPSIA (130/90+)

	PRECEDING PREGNANCY			POST PARTUM
	5-4 YEARS	3-2 YEARS	1 YEAR –	1-4 YEARS
No. of cases	7	9	14	21
Age (years)	20.4	27	26.8	29.9
Systolic (mm. Hg)	116	126.7	134.6	134.6
Standard deviation	13.0	10.6	32.4	34.3
Diastolic (mm. Hg)	79	79.2	85.7	84.7
Standard deviation	10.4	8.3	15.3	17.3

Tables IX and X present the findings in 30 patients preceding and 21 patients following pre-eclampsia whose blood pressure before pregnancy on one or more occasions exceeded 130/90 mm. Hg. There were 88 prepregnancy blood pressure readings available for study. The mean highest value ranges from 139.5 to 147.8 mm. Hg systolic and from 90.5 to 92.2 mm. Hg diastolic and the mean lowest value ranges from 116 to 134.6 mm. systolic and 79 to 85.7 mm. Hg diastolic preceding pregnancy. The maximum spread between the mean highest and lowest systolic blood pressures the same year is 23.5 mm. Hg and between the diastolic values is 12.2 mm. Hg. The spread over the five-year interval between the mean highest and lowest systolic values is 31.8 mm. Hg (116 to 147.8 mm. Hg) and between the highest and lowest diastolic values is 13.2 mm. Hg (79 to 92.2 mm. Hg). Reference to Tables IX and X shows that, with minor exception, both the mean lowest and highest values strikingly exceed those met with before a normal pregnancy. The standard deviations vary in magnitude and are consistently large in the biggest sub-group. The findings in this group are very similar, practically identical with those preceding the hypertensive form of toxemia. The mean ages are greater than that preceding normal pregnancy. The blood pressure values are higher, variable, and enter both normal and hypertensive zones. The range extends from 90 to 204 mm. Hg systolic and from 55 to 126 mm. Hg diastolic (mean plus or minus 2 standard deviations). This is also greater than that seen before a normal pregnancy. Following pregnancy and pre-eclampsia there was no actual change in mean systolic value, the standard deviation decreased from 28 to 25 when the highest value was studied, and increased from 32.4 to 34.3 when the lowest value was considered.

It may be superfluous to point out that if exacerbation of hypertension had resulted, the mean should have reflected this change and the standard deviation should have increased.

The mean highest blood pressure values in the cases of pre-eclampsia and normal pregnancy, including the number of observations for each point of reference, are charted graphically in Fig. 1. This includes a total observed course of approximately 10 years. It is clearly shown that in both normal and toxemic

pregnancy a decrease in mean blood pressure takes place at, or prior to, the third month of gestation. This follows the plateau of prepregnancy determinations. In normal pregnancy, prepregnancy values are attained between the eight and ninth months of gestation. In pre-eclampsia, which is preceded by elevated blood pressure, similar levels were reached earlier at the seventh month. In pre-eclampsia, with normotensive prepregnancy readings, maximum values resulted later. Because of premature delivery, there are fewer observations at the eighth and ninth months of pregnancy. Diastolic determinations behave in the same way. The blood pressure value reached its prepregnancy level, in each instance, following pregnancy.

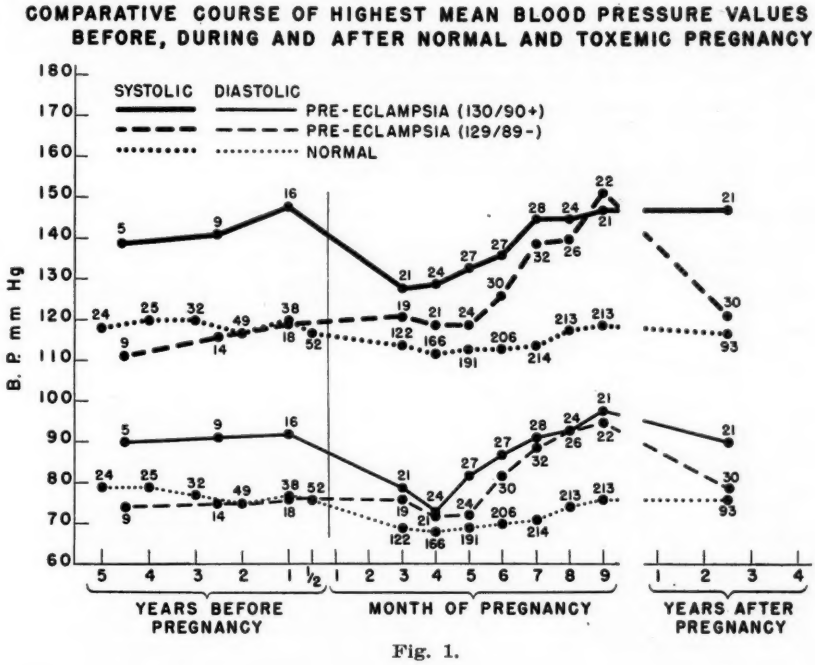

Fig. 1.

A direct comparison of the blood pressure curves among the various forms of toxemia is pictured in Fig. 2. The same relationships are evident except for the slower attainment of the pre-pregnancy value in the hypertensive form of toxemia.

As only 137 examples of toxemic pregnancy furnished the data upon which these conclusions were based, it was decided to widen the study through the inclusion of strictly comparable cases with unknown prepregnancy blood pressures. The accumulation of these cases also proved difficult.

The criteria for normal pregnancy previously described were meticulously followed, and, in addition, included a minimum observation period of at least the last four months of pregnancy, labor, and six days of the puerperium.

The hypertensive group consisted of those patients in whom the blood pressure reached on at least three occasions 130/90 mm. Hg, and did not exceed 150/99 mm. Hg. One reading of 160/100 mm. Hg was permitted. A minimum of the last four months of antepartum observation was required. Many cases had more. If the blood pressure rose in labor, the case was excluded. Proteinuria of 1 plus on three occasions was cause for rejection. This type of case was chosen although it was realized that the criteria for hypertensive disease were minimal; because these cases are relatively frequent, their homogeneity as

measured by blood pressure levels was assured, and return of these patients to the clinic because of symptoms of hypertension was unlikely.

In an effort to verify the previously noted effect of pre-eclampsia, only the most severe examples during the first pregnancy were chosen. An observation period of at least two months preceding the onset of hypertension exceeding 160/100 mm. Hg, proteinuria 4 plus, and generalized edema were required, in addition to postpartum follow-up observations. Cases of eclampsia observed in the first pregnancy with suitable follow-up were also compared, and because of the few cases available every case was used regardless of the period of antepartum observation.

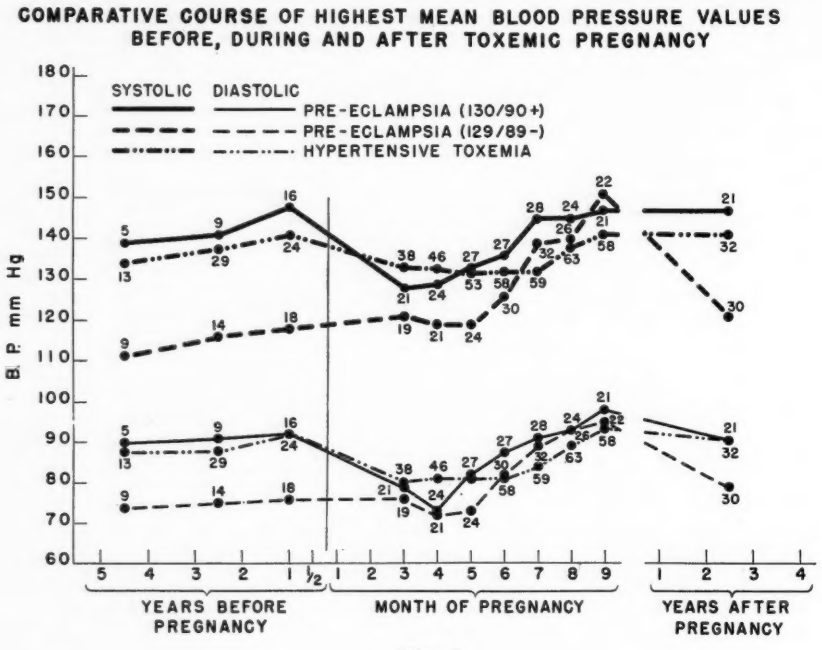

Fig. 2.

Table XI summarizes the findings in these groups. The level of hypertension adopted was 150/90 mm. Hg or higher. A systolic blood pressure of 150 mm. Hg, unless associated with a diastolic level above 90 mm. Hg, was disregarded.

As was expected, patients with normal pregnancy, regardless of whether the blood pressure was known or unknown prior to that pregnancy, had identical mean blood pressures post partum. These patients, although normotensive within the limits previously discussed, exhibited hypertension within 1 to 4 years following delivery in 1 to 2 per cent of the cases.

Patients with the purely hypertensive form of toxemia showed a significant incidence of postpartum hypertension (standard error of the difference equals 3.4 and 3.3). The difference in the incidence of later hypertension (31 per cent and 18.5 per cent), while marked percentagewise, is not significant (standard error of the difference equals 1.3) and must be the result of selection, if it is recalled that the criteria of the mild hypertensive group, including many borderline levels of hypertension, excluded severe hypertension. On the other hand, those cases of hypertension in which the prepregnancy blood pressures were known included all levels of blood pressure above 130/90 mm. Hg. The infer-

ence seems valid that both forms of toxemia, mild and severe, are related, and that the characteristics of the blood pressure determinations, in the prepregnancy phase, other than range, are identical.

In all groups of patients, where the mean value of the blood pressure was known before, there was no observed alteration following pregnancy. The assumption that a similar event results in those groups of patients whose blood pressure before pregnancy was unknown therefore seems justified. Consequently, the evidence indicates that patients with normal pregnancy began the pregnancy with blood pressures in the normotensive range, and that patients with the hypertensive form of toxemia began the pregnancy with higher levels of blood pressure.

TABLE XI. MEAN BLOOD PRESSURE VALUES AND INCIDENCE OF HYPERTENSION IN CASES OF NORMAL AND TOXEMIC PREGNANCY OBSERVED PRECEDING, DURING, AND FOLLOWING PREGNANCY

NO. OF CASES	PREPREGNANCY BLOOD PRESSURE (UP TO 5 YEARS)	PREGNANCY	FOLLOW-UP (1-4 YEARS)		HYPERTENSION	
			NO.	BLOOD PRESSURE	NO.	%
218	116.8-120.0 / 76.1-78.8	Normal	93	116.7 / 76.2	2	2.2
100	?	Normal	100	116.8 / 74.1	1	1.0
66	134.4-141.0 / 87.5-92.1	Hypertension	32	140.9 / 90.8	10	31.0
70	?	Mild hypertension	70	135.2 / 85.0	13	18.5
41	110.8-118.6 / 73.6-76.1	Pre-eclampsia and eclampsia	30	121.5 / 78.8	2	6.6
30	139.5-147.8 / 90.5-92.2	Pre-eclampsia	21	147.0 / 90.4	6	28.5
61	?	Severe pre-eclampsia	61	124.0 / 79.5	4	13.0
15	?	Eclampsia	15	131.7 / 80.0	3	20.0

When the pre-eclampsia groups are examined, the same relationships are noted. Patients with normotensive readings prior to a pre-eclamptic pregnancy had hypertension in 6.6 per cent of the cases in the follow-up. This does not differ significantly from the percentage seen following normal pregnancy (standard error of the difference equals 0.9). Those patients with pre-eclampsia whose blood pressure before pregnancy exceeded 130/90 mm. Hg had an incidence of postpartum hypertension of 28.5 per cent. This is of statistical significance (standard error of the difference equals 2.6).

As described earlier, pre-eclampsia was divided into two groups, dependent upon the prepregnancy blood pressure. When this is accomplished, one group is found nearly identical with normal pregnancy, the other with hypertensive toxemia, in regard to mean blood pressure preceding, and mean blood pressure and incidence of hypertension following, pregnancy.

The pre-eclamptic group, selected on the basis of the most severe examples of the disturbance available, but with unknown prepregnancy blood pressure, had an incidence of 13 per cent hypertension following pregnancy. These cases

were composed of an undetermined number of normotensive and hypertensive subjects. The expected incidence of late hypertension in these cases should be greater than is seen in patients with normotension and less than that seen in patients with hypertension preceding pregnancy. Reference to the tables shows that this occurred.

Conclusions cannot be reached concerning the interrelationship of eclampsia and blood pressure on the basis of the few cases available. Consequently, this study because of lack of data cannot rule out the possibility that hypertension follows eclampsia. It should be pointed out, however, that until the convulsion per se is shown to be a "hypertension instigator," the laws which apply to severe pre-eclampsia must apply similarly to eclampsia.

Conclusions

1. Studies of the interrelationship of blood pressure and toxemia of pregnancy are subject to sources of error which result from characteristics of the blood pressure measurement.

2. These characteristics briefly stated are: (a) lability in normal and abnormal range, (b) the association of a temporary elevation of blood pressure with future sustained elevation, (c) the lack of a universal definition of the lower limit of hypertension.

3. This investigation was a longitudinal study of 240 patients who underwent a normal first pregnancy and 137 patients who experienced toxemia in their first pregnancy. The range of observation varied from 21 months to 10 years.

4. Normal pregnancy is preceded in 90 per cent of the cases by blood pressure values below 129/89 mm. Hg, a mean blood pressure of 116.8 to 120.0/76.1-78.8 mm. Hg, and a range of 86 to 151 mm. Hg systolic and 48 to 100 mm. Hg diastolic.

5. The standard deviation and mean blood pressure in these cases show no change within 1 to 4 years post partum.

6. Hypertensive toxemia is preceded by a mean blood pressure of 134.4-141.6/87.5-92.1 mm. Hg (the suspiciously hypertensive zone) and a range of 92 to 180 mm. Hg systolic and 55 to 119 mm. Hg diastolic, within a year preceding pregnancy.

7. The standard deviation and mean blood pressure of these patients with hypertensive toxemia show no change within 1 to 4 years post partum.

8. Patients with pre-eclampsia show prepregnancy blood pressure values which fall into both normal and hypertensive range.

9. The standard deviation and mean blood pressure levels of patients with pre-eclampsia show no change when compared with the prepregnancy levels within 1 to 4 years post partum.

10. Blood pressure values decrease in the first and second trimesters in normal and toxemic pregnancy.

11. The woman undergoing a normotensive pregnancy is essentially a normotensive individual. The woman who exhibits hypertension solely in pregnancy was hypertensive prior to pregnancy. The patient who exhibits the pre-

eclamptic syndrome in pregnancy (hypertension, albuminuria, and edema) may have been either normotensive or hypertensive before pregnancy, and her postpartum blood pressure will reflect her prepregnancy state.

12. The duration and severity of toxemia of pregnancy are not factors in the production of posttoxemic hypertension.

13. Toxemia of pregnancy does not permanently increase hypertension.

14. The unrecognized hypertensive state is responsible for the appearance of hypertension following toxemia of pregnancy in the vast majority of cases. This lack of recognition results in part from the variability of blood pressure and the drop of blood pressure in early pregnancy.

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POSTABORTAL SEPTICOTOXEMIA DUE TO CLOSTRIDIUM WELCHII*

Seventy-Five Cases From the Maternity Hospital, Santiago, Chile, 1948-1952

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THE occurrence of postabortal infections due to *Clostridium welchii* is a relatively rare occurrence in the United States. In a recent report of 6 cases from Bellevue Hospital, the incidence of such infection was one in every 781 cases of abortion.[5] At the Maternity Hospital in Santiago, Chile, it occurs two and one-half times as frequently. From 1948 to 1952, 23,000 patients with abortion were admitted to this hospital; 75 had *Clostridium welchii* infections, an incidence of 1 in 307 cases of all abortions. Since this is an unusually large series of such cases, it seems of interest to present them.

Cases of *Clostridium welchii* sepsis were first described at the end of the last century. In 1935 Pons[11] summarized the then known cases; in 1936 Mondor[8] commented on the important aspects of this disease. The first report in the Chilean literature on this disease was by Matus and Sanhueza[7] in 1936; later publications appeared by Albertz,[2] Moreno,[9] and Puga and Rodriquez.[12] Tisne[16] presented several articles on this disease from 1938 to 1943.

Trivelli[18] in 1943 did research studies with this organism in rabbits and discovered that the hematological picture as seen in human beings could be experimentally reproduced in the rabbit solely by injections of desiccated *Cl. welchii* toxin. The conclusion was that the septicemia is not necessary for the hematological picture that develops.

The bacterium, *Clostridium perfringens* or *Bacillus welchii,* was discovered independently in three countries during 1892 and 1893, being described by Welch, Frankel, Veillon, and Zuber.[14] It is an anaerobe that ferments sugars, producing large quantities of gas of a characteristic odor.[6] It is a saprophytic inhabitant of the intestinal tract and may be a harmless saprophyte of the female genital tract.

Some observers believe that there is some factor that must be present to allow this organism to invade the blood stream and cause the septicemia and toxicity that occur. As evidence for this contention is the fact that in one series 35 per cent positive cultures for *Cl. welchii* were found in tissue removed from products aborted where the clinical courses had been mild.[3] Apparently favorable circumstances must be present to allow the organism to become virulent and produce the fulminating clinical picture that sometimes occurs.

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Clinical Description

Of the 75 cases to be presented, all but 4 patients admitted to abortive manipulations. The method most commonly used was the insertion of a rubber urethral catheter into the uterine cavity (64 per cent); in 20 per cent of the cases uterine irrigations were administered and in the remaining cases other miscellaneous objects were inserted into the uterine cavity.

When infection with *Cl. welchii* occurred, symptoms appeared in twenty-four to forty-eight hours after manipulation in 85.3 per cent of the cases and in the more acute cases within twenty-four hours. The onset was characterized by violent, shaking chills, generalized bodily aching, retching and vomiting, and diarrhea. The temperature rose quickly to high levels, but was soon followed by subnormal temperatures, hypotension, and an elevated pulse (100 to 120). A dark, putrid, foul-smelling vaginal discharge was present on admission in 89.3 per cent of the cases. The clinical course quickly assumed alarming proportions; on admission to the hospital 75 per cent of these patients were already classified as gravely ill.

Within hours after the onset of symptoms the most characteristic sign of this disease appeared—icterus.[15] Ninety-two per cent of the patients already had this icterus on admission and the remaining 8 per cent developed it to a milder degree during the course of their illnesses. This icterus was of a characteristic bronze color; sometimes it presented a greenish tinge and occasionally resembled cyanosis. In the patients who survived, the icterus disappeared within eight to ten days to be followed by an intense anemia and pallor. The urine also presented a characteristic dark brown, mahogany color.

Generalized myalgias, neuritic and joint pains, and other signs of hypersensitivity occurred. In some patients the attacks of vomiting were uncontrollable; in others the attacks of diarrhea were most severe. Oliguria occurred in 94.6 per cent of the cases with urinary outputs of 200 c.c. or less daily; anuria occurred in 23 cases (30 per cent).

The course of this disease might be described as occurring in two phases, the icterohemolytic syndrome and the hepatorenal syndrome. The first phase usually lasted from five to eight days. If the patient survived this stage, the hepatorenal syndrome followed with uremia and frequently with death. In the more acute cases both syndromes occurred simultaneously and the patient died quickly. In the more slowly progressive courses, the patients recovered after long weeks of treatment.

In more than half of the cases the total duration of the disease was eight days or less; in 21.3 per cent it lasted nine to fifteen days, and in 16 per cent sixteen to thirty days; 2.1 per cent of these patients had total illnesses of more than thirty days. The longest hospital stay was seventy days; the shortest fifteen minutes.

When death occurs with *Clostridium welchii*, it is due to the toxins elaborated by this organism, which injure the vital organs, the liver, kidneys, and blood vessels. These toxins are described as a hemolytic toxin, a necrotizing toxin, a neurotoxin, and a myotoxin. The hemolytic toxin produces the icterus, hemoglobinemia, and hemoglobinuria. The necrotizing toxin injures the blood vessels, the renal epithelium, and the hepatic epithelium. The effect on the blood vessels produces various hemorrhagic phenomena as hematemesis, melena, epistaxis, gingival bleeding, etc. The neurotoxin may lead to death in 24 hours if it affects the vital nerve centers. The myotoxin produces the muscular aches and pains, cramps, and the hypersensitivity.

The mortality rate for this series was 73.3 per cent. The outcome of these cases is classified in Table I.

TABLE I

	CASES	PER CENT
Hyperacute (death within 24 hours)	7	9.4
Acute (death before 15 days)	32	42.6
Subacute (prolonged with fatality)	16	21.3
Benign (prolonged with recovery)	20	26.7

Of the 23 patients who developed anuria, 14 died in anuria, 6 after one day of anuria, 4 after two days, and the remaining 4 after three, four, five, and six days of anuria. Nine patients recovered from anuria, 6 after the second day of anuria and 3 after the third day. The return of urinary function did not assure a favorable outcome, however; 6 of the 9 patients subsequently died. The causes of death were listed as postoperative shock and uremia, cerebral edema and uremia, pneumonia and uremia, toxic nephrotic necrosis and uremia, cardiovascular collapse, and pulmonary edema. The 3 patients who survived had anuria for two days each.

The most frequent complications that occurred among the fatal cases were necrotizing nephritis (34.6 per cent), neurotoxic disorders (13.3 per cent), generalized peritonitis (5.5 per cent), uterine gangrene (4 per cent), collapse of the respiratory organs (2.6 per cent), and enterocolitis (2.6 per cent). These complications also occurred among the survival group, but in a milder form.

Laboratory Findings

The marked anemia which was present was reflected in decreases in the red blood cell counts of 600,000 to 300,000 daily, counts of 2 million or less and varying depressions in the hemoglobin being common. This anemia was of the hemolytic, hyperchromatic, microcytic type. The serum presented a brilliant red color due to the hemoglobinemia. Leukocytosis was the usual finding with white blood cell counts of 20,000 to 40,000, a shift to the left, and degenerative changes in the neutrophils. The platelet counts varied; diminutions in the counts occurred in 50 per cent of the cases. Eosinophils were not present. These changes in the blood picture are of diagnostic importance,[19] and they appear early in the disease before the blood cultures are found to be positive.[17]

In addition to the dark brown, mahogany color of the urine, albumin was always present. There was an increase in urobilin; no bile salts or biliary pigments were present. There was no characteristic urinary microscopic picture; red blood cells were observed rarely.

Blood chemistry determinations showed high bilirubin readings, fluctuating between 25 and 50 mg. per cent, increases in blood sugar, and decreases in calcium, total protein, and chloride determinations. The laboratory findings of uremia increased rapidly with kidney damage and decreased slowly as urinary function returned.

Bacteriological studies were made of the products of conception, the blood, and urine; the largest number of positive cultures were obtained from the products of conception. Negative cultures sometimes were obtained despite clinical findings of *Cl. welchii* infection. In some instances the patient's early death prevented more intensive bacteriological studies.

Pathological Findings

The most characteristic pathological feature of this disease on postmortem examination was parenchymal degeneration and rapid necrosis of the organs.

Where an intense bronze icterus was present, histological examination of the skin showed the accumulation of the blood pigments in the papillae.

The most marked pathological changes were found in the liver, spleen, kidneys, heart, and uterus. The liver usually appeared congested, friable, hemorrhagic, and gas escaped from it on sectioning. Microscopically, albuminoid or granular degeneration was evident with small necrotic foci and sometimes gas present in the form of small vesicles. The spleen usually appeared friable, with no change in its weight. The kidneys were always edematous, with a smooth surface, of a violet or brownish red color. The microscopic changes were most evident in the tubules with tumid and necrotic cellules and containing numerous casts of hemolyzed blood. In the interstices edema and polynuclear infiltration were present. The glomeruli appeared hyperemic. The heart revealed a cloudy degeneration on microscopic examination.

The uterus usually appeared soft and friable. An inflammatory infiltration was evident between the muscle bundles which in some more advanced stages was associated with a purulent peritonitis.

Treatment

The basic principles in the treatment of these postabortal infections with *Cl. welchii* were the rapid removal of the infectious focus, the neutralizing of the circulating toxins, and the supportive treatment of the functions of the vital organs damaged by toxins.

Emptying of the uterus by dilatation and curettage was done in 67 of the 75 cases (47.7 per cent in the first twenty-four hours, 52.3 per cent in 48 hours or later). Hysterectomy is deemed advisable where damage to the uterine wall is present or suspected.[1] Hysterectomy was not done in any of these cases; the remaining 8 patients were in too grave a condition to withstand any operative procedure.

The specific treatment employed in 53 cases (70.7 per cent) was the administration of the Perfringens antitoxin. This product is prepared in the Bacteriological Institute of Chile, where the concentrated and dyalized serum has been prepared since 1937. In 1940, Poppe's modified method of preparation, which prevents shock or serum sickness, has been followed. The serum is sold in ampules containing 10,000 I.U. of Perfringens antitoxin, at a cost of 320 Chilean pesos ($3.00). For an individual patient the cost for adequate antitoxin treatment was about $300.00.

Two hundred thousand international units of the antitoxin were given daily, 50,000 I.U. every four to six hours, either intravenously in physiological solution or intramuscularly, for four to six days. Local intrauterine antitoxin treatment was also administered in some cases.

The antibiotics were also administered.[10] Penicillin was given in 82.6 per cent of these cases and streptomycin in 24 per cent. During 1948 and 1949 the dosages of penicillin were low and were subsequently markedly increased.

The supportive treatment consisted of the administration of intravenous solutions of sodium chloride, oral or intravenous solutions of sodium bicarbonate, 2 per cent Novocain in physiological solution as a glomerular dilator, adequate hydration, 30 per cent glucose solution intravenously, whole blood transfusions (in 32 per cent of the cases), cardiovascular stimulants, high-protein diets along with vitamins B, C, and K, and intraperitoneal irrigations for peritoneal dialysis to detoxify the uremic patient.

Renal decapsulation was performed in 10 cases; only one of these patients survived. This procedure used to be highly recommended in cases of edema

of the kidneys to relieve the pressure within the capsule of the kidney. It does not appear to be of much help, however, and is no longer advised. Spontaneous diuresis is established when and if the renal epithelium regenerates.

All patients received some degree of supportive therapy, and in most instances antibiotic therapy. The 53 patients who received antitoxin therapy also had curettage done. Fifteen of these 53 patients survived, a 28.3 per cent survival rate. Of the 22 patients who did not receive antitoxin treatment, 14 had curettage done. Five of these 22 survived, a survival rate of 22.2 per cent.

Sixty-nine per cent of the 55 patients who died had received antitoxin therapy. The remaining 31 per cent did not receive it because it was not available (the cost was a factor) and because of the grave condition of the patient on admission. Seventy-five per cent of the 20 patients who survived had received antitoxin therapy.

The success of the treatment with antitoxin appeared to be related to the time interval which had elapsed from the onset of symptoms to the administration of the antitoxin. When it was given within twenty-four hours after the onset of symptoms the survival rate was 38.4 per cent. When symptoms had been present for four or more days before its administration, there was a 7.8 per cent survival rate.

After reviewing the results of treatment, the outcome appeared to depend for the most part on the degree of toxicity and virulence of the organism involved in any given case. Some of the patients with the mildest forms of this disease recovered with scant or little treatment. Despite hemoglobinuria and icterus, if the urinary output was at least 500 c.c. daily, the prognostic outlook was brighter. If the urinary output increased, but its concentration did not improve, the uremia persisted and the patient died.

Even with prompt treatment as outlined, the salvage rate was only 26.7 per cent. Some statistical studies have reported even better results.[4, 5] Before the use of the antitoxin, the antibiotics, and the removal of intrauterine infectious material, however, the mortality rate at this hospital was almost 100 per cent. Thus the mortality rate has been reduced to 73.3 per cent with this treatment; the results later in the series were better than in the early years of the study. These figures are given in Table II.

TABLE II

YEAR	NUMBER OF CASES	NUMBER WHO DIED	PERCENTAGE MORTALITY RATE
1948	8	7	87.5
1949	12	10	83.3
1950	26	19	73.0
1951	13	8	61.5
1952	16	11	68.7
Total	75	55	73.3

Comment

The medical profession in Chile is fully cognizant of the very serious problem of induced abortions there. Approximately 5,000 cases of abortion are admitted yearly to the Maternity Hospital in Santiago which is the largest such hospital in South America and has a yearly admission of 12,000 patients.[13] In most of these admissions for abortion a criminal abortion has been attempted, and the incidence of infection with *Cl. welchii* is as reported. Twenty-three per cent of all deaths in this hospital were due to this type of postabortal infection.

Although better therapeutic measures are sought to attempt to control this disease, the real approach should be directed at the whole abortion problem there. Criminal abortion is deemed illegal, but the patients offer "economic and personal" reasons for their actions. Sixty-eight per cent of the 75 patients were married.

The problem is basically one of the socioeconomic conditions which nourish it. The type of manipulation which is the least expensive and simplest to obtain is usually employed and carries the highest fatality rate. Prevention of this disease might be directed toward more severe legal punishment for those performing these criminal abortions, and, more importantly, toward raising the standards of living for these people.

Summary

1. Seventy-five cases of postabortal infection with *Clostridium welchii* are presented. These occurred from 1948 to 1952 at the Maternity Hospital in Santiago, Chile.

2. The incidence of this infection at this hospital among all patients with abortion was 1 in 307.

3. The symptoms and clinical course of these cases are described. The diagnostic triad of hemoglobinuria, hemoglobinemia, and a deep bronze icterus leaves no difficulty in the diagnosis of this disease.

4. The course of the disease is described as occurring in two phases, the icterohemolytic syndrome and the hepatorenal syndrome.

5. The mortality rate was 73.3 per cent, with a decrease in mortality rate from 87.5 per cent early in the series to 68.7 per cent in the last year.

6. Twenty-three (30 per cent) of these patients developed anuria; 94.6 per cent had oliguria some time during the course of their illnesses.

7. Laboratory and pathological findings are described.

8. Treatment was directed along three basic lines, removing the focus of infection in the uterus, specific treatment with Perfringens antitoxin and antibiotics, and supportive treatment.

9. Although the outcome of any given case depended primarily on the virulence and toxicity of the organism, treatment as outlined appeared to offer a better chance of survival.

10. The serious abortion problem in Chile is decried and a plea for preventive measures to curtail it made.

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THROMBOTIC THROMBOCYTOPENIC PURPURA OCCURRING IN PREGNANCY

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APPROXIMATELY fifty cases of thrombotic thrombocytopenic purpura have appeared in the literature since the first case was reported by Moschcowitz[1] in 1925. To date no record of this rare syndrome during pregnancy has been reported, although there is a high incidence of this condition in women of the childbearing age.

Thrombotic thrombocytopenic purpura is a clinical entity of unknown etiology characterized by fever, hemolytic anemia, mild icterus, thrombocytopenia, and central nervous system manifestations,[2] including headache, mental confusion, delirium, coma, convulsions, aphasia, and hemiplegia.

Postmortem examinations have disclosed multiple acellular thromboses in the smaller arterioles and capillaries. These characteristic lesions are widespread and are found most frequently in the heart, lungs, adrenals, kidneys, and brain. The degree of involvement of these organs varies with each case.

Baehr and associates[3] first suggested the possibility of an allergic etiology because of the microscopic picture of the vascular lesions. Subsequent authors[4, 5, 6, 7] have noted urticaria and drug sensitivity in the cases they have reported. Barondess[8] presented a comprehensive review of the literature. Evidence of a past history of hypersensitivity was present in 8 of 32 cases he reviewed.

We feel the following case report is of interest because of the occurrence of this rare disease during pregnancy. The difficulty in differentiating thrombotic thrombocytopenic purpura from glomerular nephritis, lower nephron nephrosis, acute leukemia, and toxemia of pregnancy is illustrated by this case.

Case Report

A 19-year-old primiparous white housewife in the eighth month of pregnancy was admitted to the obstetrical ward of the Mountain Home Air Force Base Hospital, on April 18, 1954, complaining of headache, generalized edema, nausea, vomiting, and lower abdominal cramps.

The patient's past history was noncontributory. The family history failed to disclose any significant hematological or renal abnormalities. The patient's last menstrual period began on Aug. 9, 1953. In October, 1953, because of repeated infections, a pilonidal cyst was excised. A complete blood count, bleeding time and coagulation time determinations, serologic test, and routine urinalysis were done prior to operation and were all within normal limits.

At her first prenatal check-up in mid-December, 1953, she reported a slight, intermittent, bloody vaginal discharge of three weeks' duration. Physical examination showed a healthy young woman in the fourth month of pregnancy. Chest x-ray, blood counts, serologic test, and urinalysis were normal. She was given progesterone and advised to rest in bed. The bleeding stopped and the pregnancy was uneventful until March 25, 1954. At this visit to the prenatal clinic she complained of burning pain on urination. A urinalysis showed innumerable white blood cells per high-power field and 5 to 10 red blood cells. After a short course of Mandelamine the urinary symptoms subsided.

One week before admission to the hospital the patient noted swelling of the ankles which increased and spread to the hands and face. She also noted a decrease in urinary output. Two days prior to admission she developed generalized weakness and headache.

Physical examination on admission disclosed a pale, nervous 19-year-old white girl with generalized body edema. She was vomiting and in active labor. The pulse rate was 68 per minute and regular and respirations were 20 per minute. The blood pressure was 138/90; throughout pregnancy the blood pressure had been approximately 110/75. The lungs were clear to percussion and auscultation. No cardiac enlargement was noted but the patient had a soft apical systolic murmur. Abdominal palpation showed the uterine fundus to be 4 cm. above the umbilicus. The membranes had ruptured just prior to admission to the hospital. The patient had a moderate flow of bright red blood from the vagina. There was 3 plus pitting edema of the feet, legs, hands, and forearms.

On the evening of admission the urine showed 4 plus albuminuria. The patient was given 100 mg. Demerol which failed to decrease her nervousness. She vomited dark green fluid frequently and had a moderate amount of vaginal bleeding. Two hours after admission she was given 2 c.c. of 50 per cent magnesium sulfate intramuscularly. Shortly afterward she spontaneously delivered a viable 3 pound, 12 ounce, infant. After delivery the patient's irritability greatly diminished and she slept quietly for six hours.

On the following day the blood pressure had fallen to 108/82. The urine output for the second hospital day totaled over 3,500 c.c. She was now on a salt-free diet and, although nauseated, she did not vomit. She coughed up a small amount of clear mucus slightly streaked with blood. A blood count showed 10.5 Gm. of hemoglobin per 100 ml., and 8,750 white blood cells with 68 per cent neutrophils, 4 per cent band forms, 23 per cent lymphocytes, 3 per cent monocytes, and 2 per cent basophils.

On the morning of the fourth hospital day the patient complained of a moderately severe headache. The obstetrician noted that she was unable to recall the early morning visit of her husband and showed a definite loss of memory for recent and past events.

A medical consultation was obtained. On examination there was a marked pallor of all mucous membranes with a café-au-lait complexion, uriniferous odor to the breath, a flame-shaped hemorrhage in the left optic fundus, petechiae on the soft palate, a few ecchymotic areas in the antecubital fossae at needle sites, tenderness bilaterally over the costovertebral angles, and a firm uterus with the fundus 3 cm. below the umbilicus. A neurological examination was negative except for memory defect.

A blood count on the fourth hospital day showed 9 Gm. of hemoglobin with 1.9 million red blood cells. The nonprotein nitrogen was 75 mg. per cent. Therapy was started and included penicillin, blood, and oxygen. On the following day the patient had no memory defect or headache. Urinary output remained high and a diminution of the edema was noted. The nonprotein nitrogen dropped to 64 mg. per cent. The urine continued to show albuminuria and numerous red blood cells.

She received blood transfusions from the fourth through the eighth day. These transfusions had very little effect on the hemoglobin or red blood cell level (Fig. 1). On the sixth and seventh hospital days the patient, although pale, slightly icteric, and weak, evidenced no memory defect. It was noted that the blood pressure gradually increased during these days.

On the eighth hospital day the patient complained of a frontal headache and again became unable to recall recent or past events. Her temperature was now 100° F. and blood

pressure 140/90. Later in the day she vomited in a projectile manner, became aphasic, and was unable to move the right upper and lower extremities. She was found to have bilateral ankle clonus and positive Babinski signs. The nonprotein nitrogen on the eighth day was 90 mg. per cent. Nucleated red blood cells were seen on a blood smear.

On the morning of the ninth hospital day, the patient was comatose, the temperature 101.2° F. rectally, and the pulse rate 100. The skin was pale and icteric with no ecchymoses or petechiae. The pupils were dilated and there was a lateral nystagmus. There were a few scattered moist râles over both lungs. The heart sounds were regular and no murmurs could be heard. The blood pressure was 160/100. She had 1 plus pitting edema of the feet and ankles. Although she had a right hemiplegia, the right hand moved a little on stimulation.

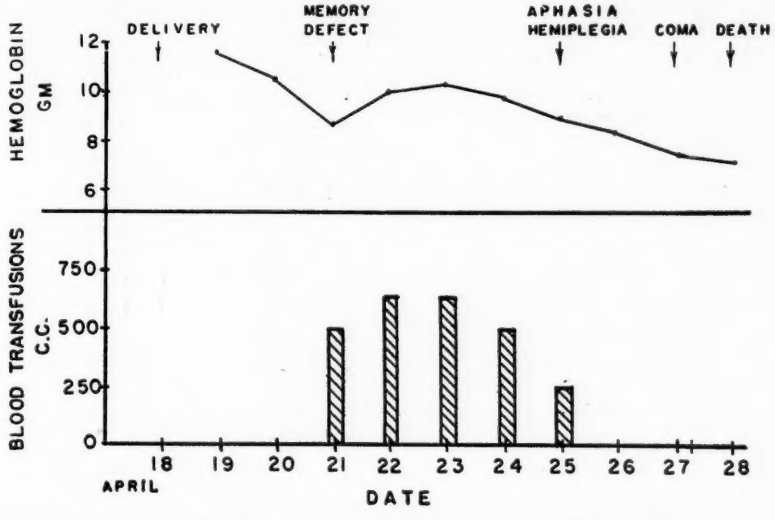

Fig. 1.—Graph of hemoglobin and blood transfusions. Note the falling hemoglobin in spite of repeated transfusions.

Laboratory studies included the following: hemoglobin 8.6 Gm., red blood cells 2.97 million, white blood cells 6,700, with 58 per cent neutrophils, 17 per cent stab forms, 15 per cent lymphocytes, 9 per cent monocytes, 1 per cent eosinophils, 11 per cent nucleated red blood cells, moderate poikilocytosis, marked anisocytosis, and moderate polychromatophilia. The hematocrit was 27 per cent, sedimentation rate 111 mm. in 45 minutes, blood urea nitrogen 53 mg. per cent, calcium 6.7 mg. per cent, and the carbon dioxide combining power 44 volumes per cent. The platelet count was 35,640, bleeding time 1½ minutes, coagulation time 8 minutes, prothrombin time 15 seconds with a control being the same value, and there was little clot retraction in 24 hours. The icteric index was 32, potassium 22.2 mg. per cent, and fibrinogen level 319 mg. per cent. The urine was scanty and bloody. The direct Coombs test was negative. The erythrocytes demonstrated a typical fragility curve.

The patient was given protoveratrine intravenously with reduction of the blood pressure from 160/100 to 130/90. Therapy also included continuous nasal oxygen, Digoxin, and penicillin. Tracheotomy was done to give a better airway and facilitate removal of mucus. Because of a urine output of only 350 c.c. in the previous 24 hours, intravenous solutions were limited to 1,000 c.c. of 5 per cent glucose in distilled water.

On the tenth hospital day her coma deepened, her temperature rose to 103° F. rectally. The right knee jerk was still hyperactive and the Babinski sign positive on the right but the ankle clonus was gone. The white blood count was now 20,300, blood urea nitrogen 65 mg. per cent, and the van den Bergh reaction showed 0.8 mg. direct and 1.2 mg. indirect. The urine output was 320 c.c. and she was given 500 c.c. of 10 per cent glucose intravenously on this day.

Fig. 2.

Fig. 3.

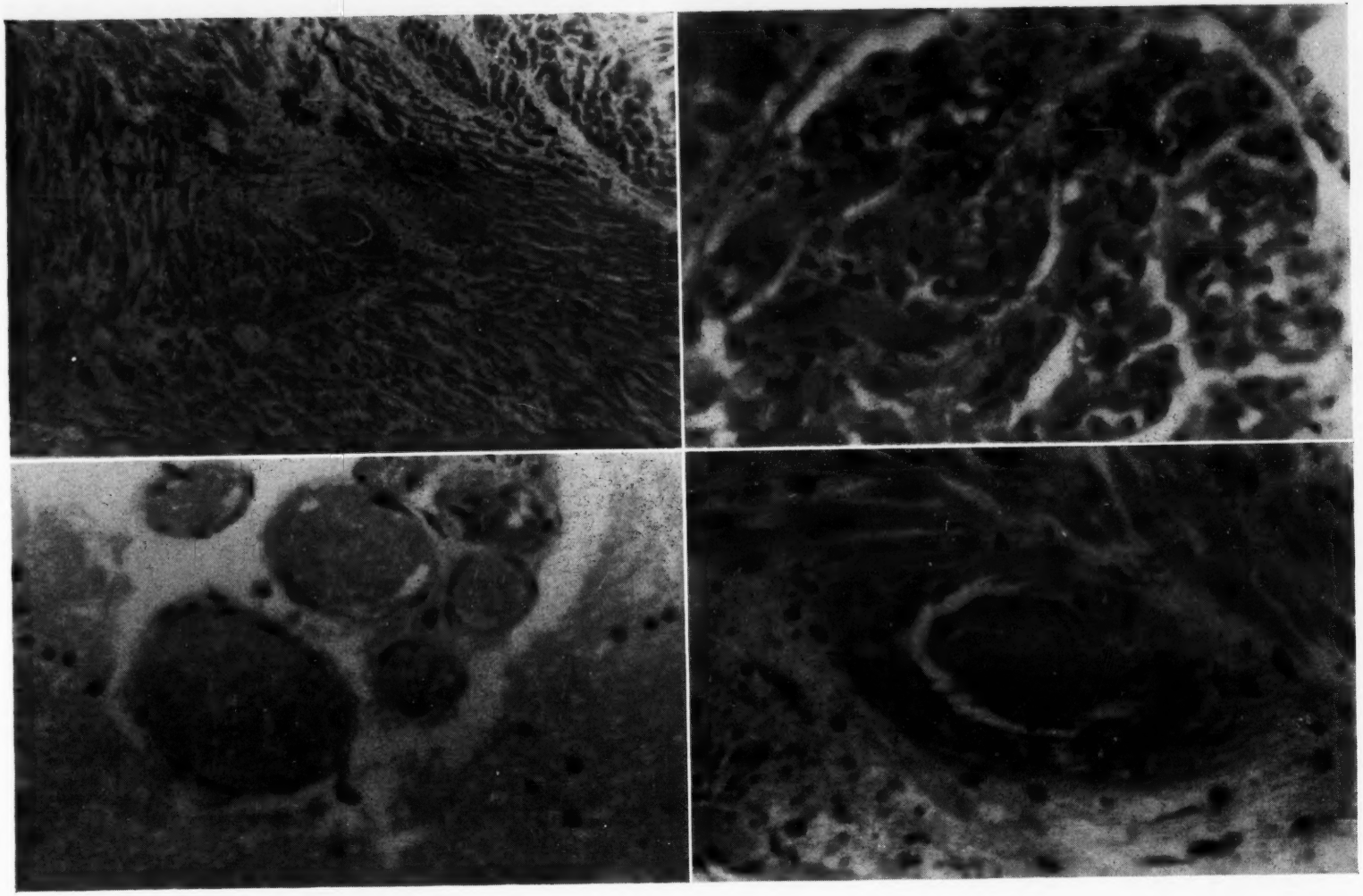

Fig. 4.

Fig. 5.

Fig. 2.—Occluded myocardial arteriole with surrounding interstitial myocardial hemorrhage. (×100.)
Fig. 3.—Multiple thrombi within glomerular capillaries. (×450.)
Fig. 4.—Bland thrombi within cerebral vessels. (×450.)
Fig. 5.—The same vessel seen in Fig. 2 demonstrating a thrombus with apparent endothelial covering. Focal necrosis within the wall and deposition of amorphous eosin-staining matter in the wall are identified. (×450.)

The patient's coma was still deeper on the eleventh hospital day; her respirations rapid and shallow. The blood urea nitrogen was now 108 mg. per cent and the carbon dioxide combining power 34 volumes per cent. She was given 1,000 c.c. of 10 per cent glucose in distilled water with 20 mg. ACTH intravenously on this day and died before the infusion could be completed.

At autopsy no hemorrhages of the skin or mucous membranes were noted. There were petechial hemorrhages involving the pericardium, endocardium, myocardium and renal cortex. Hemorrhage into the myometrium beneath the site of placental separation was extensive. The lungs were heavy and wet and tenacious mucous plugs occluded major bronchi. The brain was grossly negative.

Microscopic examination showed amorphous eosin-staining thrombi occluding arterioles, capillaries, and occasional venules throughout most of the tissues. Weigert's stain showed no fibrin matrix to these thrombi. Interstitial hemorrhage accompanied the vascular occlusion in the myocardium (Fig. 2). The lungs were markedly edematous but free of thrombi. Small foci of hemorrhage and necrosis were present in liver and adrenal cortex. The spleen showed foci of active hematopoiesis. Occlusion of glomerular capillaries (Fig. 3) and renal arterioles with thrombi was seen and there were associated petechial hemorrhages. Tubules contained numerous hyaline casts, desquamated epithelial cells, and red blood cells. There were focal areas of exudation of polymorphonuclear neutrophils within glomeruli and tubules. While the uterine wall showed extensive interstitial hemorrhage, there were no occluded vessels. Multiple thrombi were present in sections from the cerebrum (Fig. 4).

Many of the thrombi were completely bland in appearance but in several the thrombus blended with the vessel wall with no evident endothelial lining. In a few arterioles there was deposition of amorphous eosin material within the vessel similar to the thrombotic material. This was associated with hemorrhage and what appeared to be focal necrosis of vessel wall (Fig. 5). Some of the thrombi were permeated by proliferating endothelial cells.

Comment

In the few reported descriptions of thrombotic thrombocytopenic purpura the clinical triad of hemolytic anemia, thrombocytopenic purpura, and involvement of the central nervous system is usually found. These were present in this patient. Although she lacked the usual widespread purpuric skin lesions, a phenomenon reported by others[7, 9, 10, 11] she had petechial hemorrhages in the kidneys, heart, liver, and adrenals. She failed to develop the usual bleeding tendencies such as gross hematemesis, melena, or uterine hemorrhage, although she did have scanty hematuria and blood-streaked sputum.

The diagnosis in this case remained controversial throughout her illness and was in doubt until the microscopic tissue sections were examined by the pathologist. The albuminuria and moderate elevation of blood pressure suggested the possibility of toxemia of pregnancy. The absence of these symptoms during the prenatal course and the mildness of the hypertension did not give support to this diagnosis. The findings of albuminuria and increased nitrogen content of the blood served to focus attention on the kidneys, even before the onset of oliguria and hematuria. The possibility of an activation of an acute glomerular nephritis on the basis of a latent chronic nephritis was considered. The past history failed to disclose any ailment simulating nephritis.

The development of oliguria suggested the possibility of a lower nephron nephrosis on the basis of either a transfusion reaction or parturition. Of these

a transfusion reaction could not be ruled out although there had been no report of any chills, fever, or back pains during or immediately following any transfusion. The shortness of the labor and the ease of delivery without any manipulative or operative procedure, shock, or hemorrhage did not favor a tubular nephritis on this basis. Pre-eclampsia is often listed as one of the causes of lower nephron nephrosis but Young[12] believes this to be rare in the eclamptic complex. Sheehan's[13] observations on the kidney tend to implicate the glomerulus more commonly in eclampsia, while the tubules are more frequently involved in abruptio placentae.

In 1952 Barondess[8] reported this syndrome in a 42-year-old white woman who had had mild pre-eclamptic toxemia with two previous pregnancies. The onset of her illness was associated with neurological and mental symptoms. Splenectomy was done and the patient died on the fifth postoperative day. Whether the toxemias of pregnancy played any part in the etiology in our case or in the one reported by Barondess is difficult to ascertain. There are some similarities in that both patients had neurological symptoms with fever, anemia, and thrombocytopenia. Other than these features there are no striking parallels and in the case described by Barondess there was a considerable lapse of time between the last pregnancy with toxemia and the onset of the thrombotic thrombocytopenic purpura.

The differential diagnosis from other conditions causing hemolytic anemia and thrombocytopenic purpura must include idiopathic thrombocytopenic purpura and acute leukemia. The frequency of cerebral hemorrhages associated with acute leukemia has previously been reported.[14] The neurological signs in these diseases are not transitory and reversible but rapidly progressive to a fatal termination. Leukemic infiltration should have been associated with enlargement of lymph nodes and spleen and leukemic blood changes which were not present. Lupus erythematosus with predominantly renal involvement and thrombocytopenia was considered. This patient did not have a heart murmur, the skin lesions, or leukopenia usually present in lupus.

Intravascular hemolysis, thrombocytopenia, and other hematological abnormalities may be associated with severe toxemia of pregnancy.[15] At postmortem there was gross hemorrhage in the uterine endometrium and myometrium suggesting the possibility of premature partial separation of the placenta. One might speculate that this hemorrhage resulted from the bleeding tendency associated with the patient's ailment and caused the onset of premature labor.

All reported cases of this disease have progressed to a fatal termination. Splenectomy and ACTH or cortisone have been tried as therapeutic measures but have produced no striking beneficial effects. Therapy in our patient was directed at the correction of the anemia and low-grade uremia during the first few days of her illness and later with the onset of oliguria the treatment of anuria appeared to be of utmost consideration.

Therapeutic measures in this case included blood transfusions, forcing fluids, digitalis, penicillin, oxygen, protoveratrine, tracheotomy, restricting fluids, and ACTH. Blood transfusions were given for the anemia without appreciable change in either the hemoglobin or red blood count. Fluids were forced to reduce the blood nitrogen and later fluids were restricted because of the anuria. Oxygen and digitalis were given with the onset of pulmonary edema and it was hoped that the digitalization might protect the myocardium against toxicity from retained potassium. Because the obstetrician thought the patient had a toxemia of pregnancy, protoveratrine was given intravenously to reduce the blood pressure. The drug did reduce the pressure from 160/100 to normotensive levels but this probably served only to reduce the blood flow through the kidneys and hasten the patient's exitus. Tracheotomy served to give the patient a better airway and improve her breathing. ACTH was being administered intravenously when this patient died, so any possible benefit from it could not be determined.

In this patient the fatal outcome appeared to be on the basis of renal failure, although she did have the other features of thrombotic thrombocytopenic purpura, including fever, anemia, thrombocytopenia, and neurological signs. Comess and Oyamada[16] described a case of platelet-cell (thrombocyte) thrombosis associated with uremia due to malignant nephrosclerosis, acute pancreatitis, and pancreatic insular insufficiency (diabetes). Their case is apparently the only one in the literature in which the patient with this syndrome died with a significant degree of uremia. One would expect renal failure to develop in numerous cases in view of the frequency of thrombi found in the kidneys but this is apparently the exception rather than the rule.

Summary

A rapidly fatal case of thrombotic thrombocytopenic purpura during pregnancy is reported. To our knowledge no other case of this syndrome in pregnancy has previously been described in the literature. The differential diagnosis presented by this rare condition is outlined.

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THE ROLE OF N-ALLYLNORMORPHINE IN THE PREVENTION AND TREATMENT OF NARCOTIC DEPRESSION OF THE NEWBORN*

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N-ALLYLNORMORPHINE, known officially as nalorphine and commercially as Nalline, is a proved antagonist of respiratory and circulatory depression caused by morphine, Demerol, and other narcotics. The injection of 0.1 to 0.25 mg. into the umbilical vein of a newborn infant depressed by a narcotic is usually, but not always,[1] followed by prompt improvement of respiration and circulation.

Since Nalline became clinically available two years ago, enthusiastic excesses threaten to becloud its intrinsic worth and proper position in clinical practice. This warning is particularly applicable to the current fashion of depending entirely on Nalline to avoid the dangers of narcotic obstetric analgesia. Already the regular use of nalorphine with every dose of Demerol has become routine in some obstetric services.[2] In others morphine or Demerol is administered freely with the expectation of preventing neonatal asphyxia by the intravenous injection of the parturient with 10 mg. of nalorphine 10 to 15 minutes before the delivery of a potentially narcotized fetus. These practices are reminiscent of three other methods of prophylaxis against respiratory depression by drugs:

1. When thiopental anesthesia was introduced with larger doses and concentrations than we now know to be safe, Lundy of the Mayo Clinic recommended the simultaneous injection of nikethamide as the safeguard.

2. Antagonism of neonatal drug depression, with excellent results, was reported for the routine injection of 1.5 c.c. of nikethamide into the umbilical vein of 216 newborn infants whose mothers were freely sedated with Demerol and Seconal and delivered with open drop ether.[3]

3. Abel, Ball, and Harris[4] published a comprehensive study showing that amphetamine, administered intramuscularly with morphine, enabled the newborn to breathe as promptly as nonmedicated controls.

None of these methods became popular because clinicians have preferred to avoid rather than to combat the excessive use of depressant drugs.

It is now necessary to dwell on the deficiencies and dangers of routine dependence on n-allylnormorphine as a prophylactic agent:

A. Nalline is a mild narcotic capable of depressing respiration and circulation when given intravenously in a 5 or 10 mg. dose to normal subjects.[5, 6] Nalline, per se, is probably harmless in a patient free of any other depressant

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factor. But the simultaneous presence of a non-narcotic depressant, such as nitrous oxide or ether, facilitates the appearance of a synergistic or additive effect from Nalline.[1] Indeed, it is recommended that Nalline should not be administered to parturient women or newborn infants if ether is used.[1] When neonatal depression is primarily due to prematurity, cerebral trauma, etc., Nalline may significantly aggravate the depression.[1] This relationship has not yet been reported, probably because investigators have eliminated such cases.

B. Nalline is not effective in counteracting depression produced by ether, cyclopropane, or barbiturates.[1, 7, 8] Where inhalational anesthetics in addition to opiates are probably the cause of infant depression, normorphine might be considered only after artificial respiration has removed most of the anesthetic from the baby.[1]

C. Nalline, 5 or 10 mg., has little analeptic effect. Larger doses may rouse the patient but only transiently.[1]

D. Nalline increases the depression of mothers sedated with both secobarbital sodium and Demerol.[1, 6] The prolongation of depression by 15 to 30 minutes in mothers who received general anesthesia and normorphine is "undesirable since it might increase the hazard of respiratory obstruction or aspiration of vomitus."[1]

E. Inexplicable apnea of 5 minutes' duration may appear in an infant born of a mother who has received n-allylnormorphine.[1] There is suggestive evidence that the effectiveness of nalorphine disappears and that infants are actually slower in starting respiration when the drug is administered more than 25 minutes before delivery.[1] When Nalline is injected less than 10 minutes before delivery the results are uniformly poor.[9] The optimum interval of 10 to 15 minutes between intravenous injection and delivery is a difficult requirement to meet, unless the patient is under spinal or general anesthesia. The evidence cited below indicates that the administration of Nalline to the mother is unnecessary with conduction anesthesia, of doubtful value with nitrous oxide-oxygen, and possibly harmful with ether anesthesia.

F. The action of Nalline on respiration usually disappears before that of Demerol or morphine; the infant may therefore become depressed again. Even though readministration of the drug may promptly alleviate this situation, its occurrence in the nursery is an unpleasant possibility at the least. Furthermore, there is evidence that repeated doses decrease in effectiveness.[9]

G. The suggestion of Cappe, Himel, and Grossman[2] that Nalline be given simultaneously with Demerol whenever the latter was used in labor was not adequately documented. Indeed, Solomon and co-workers[9] claimed that this routine showed poorer results than when Nalline was given 10 to 20 minutes prior to delivery. Their explanation was that the beneficial effect of Nalline wears off in about 40 minutes whereas that of Demerol persists for three hours.

H. Nalline, administered to the mother as a prophylactic against neonatal depression, has not yet been tested under conditions completely satisfactory for statistical significance. All of the groups have been too small; many factors have not been controlled or studied.

The most complete study to date is that of Eckenhoff, Hoffman, and Funderburg[1]; their results must be carefully considered. Ten milligrams of nalorphine was routinely injected into opiate-sedated parturients 4 to 25 minutes before delivery.

1. Under regional anesthesia there was no statistically significant improvement in the newborn infant's "time to gasp" or "time to establish respiration" or in the frequency of "required resuscitation"; the incidence of "prophylactic resuscitation," however, was decreased.

2. With nitrous oxide and at least 20 per cent oxygen, in lightly narcotized mothers, nalorphine was of no value by any criterion.

3. When ether was added to nitrous oxide-oxygen, the "time to gasp" and "time to establish respiration" were unchanged by Nalline; infants in the Nalline-treated group were more narcotized; resuscitation was applied in 24 per cent of these and in 19 per cent of the control group, a difference that was not statistically significant in the 221 patients in this series.

4. The beneficial effect of nalorphine was apparent only when the mother was moderately or deeply depressed and the anesthesia was nitrous oxide-oxygen. Differences in the "time to gasp" and the "time to establish respiration" were significant. The incidence of "required resuscitation" was lower in the treated group (significantly, according to the authors, but not by my own calculation with the chi-square formula).[10] At any rate, 11.6 per cent of infants born of the Nalline-treated parturients received "required resuscitation" and an additional 5.8 per cent received "prophylactic resuscitation."

5. An observation common to all of the Nalline-treated narcotized group was that the "time to initial respiration (gasp)" and the "time to establish respiration" were never reduced by Nalline to equal the corresponding "times" of non-narcotized controls.

6. The only highly significant difference (my own calculation) in the entire study of 1,100 parturients was in the lesser need for "prophylactic resuscitation" of babies born of Nalline-treated mothers under regional anesthesia. The frequency of "required resuscitation" was not significantly different (my own calculation) between treated and control groups in any of the various categories of sedation and anesthesia studied.

These results are confirmed by the only other comparable published study, that of Solomon, Michael, and Siegel.[9] They injected 10 mg. of Nalline intravenously 10 to 20 minutes before delivery of 65 parturients under Demerol analgesia and various types of anesthesia. No statistically significant difference in the frequencies of "delayed breathing" and "delayed crying" was found between the treated group and the 58 controls. There was a highly significant decrease in the need for prolonged resuscitation in the treated group. Nevertheless, cyanosis was evident in 18 per cent of the 50 Nalline cases in their "corrected data," after careful screening of cases to avoid obstetric or anesthetic conditions which, in common practice, complicate delivery and tend to interfere with the benefits of Nalline.

I. Normorphine probably has its most practical and dramatic value when 0.1 to 0.25 mg. is injected directly into the narcotized newborn infant via the umbilical vein. This is the tentative conclusion of the two authors of the detailed reports previously analyzed.[1, 9] In a specific study of this route, Paterson and Prescott[11] gave 0.5 mg. to 28 narcotized infants 10 seconds after birth. Respiration always occurred within 2 minutes; in 90 per cent the time inter-

val was only one-half minute. Impressive as these figures may seem the authors were careful to point out that these observations were not controlled since they waited only 10 seconds before injecting nalorphine into the umbilical vein. "Statistically it could not be shown that nalorphine materially altered the time taken by the baby to cry." It is equally important to realize that these 28 nalorphine-treated babies failed to cry for a long period, which frequently was 15 minutes, and occasionally was 18 minutes. During this prolonged state of drowsiness 43 per cent of the treated infants required continuous active resuscitative efforts with oxygen, analeptics, and artificial assistance to breathing. In fact, with the "time to cry" as the criterion there was no definite statistical difference between the controls and the nalorphine-treated babies. The only significant difference was that active resuscitation was required in only 43 per cent of the treated group as compared with 91 per cent of the nontreated controls.

J. Under cover of nalorphine, Demerol or other narcotics are used more freely in labor. This effect demands more careful anesthesiologic observation of parturients during the profound narcosis before and after delivery and requires the avoidance of general anesthesia during delivery. Paradoxically, however, when general anesthesia is not used, Nalline is not really necessary, as shown earlier in this report. Indeed, the relatively benign effect of Demerol on neonatal respiration after delivery *without general anesthesia* has long been recognized. Even without nalorphine the incidence of neonatal depression has been relatively low, e.g., 7 per cent,[12] 9 per cent,[13] 14 per cent,[14, 15] 15 per cent,[16] 16 per cent,[11] 21 per cent.[17] The marked variations probably depend mainly on the diagnostic criteria of neonatal asphyxia and the anesthetic method at delivery. *Neonatal death due directly and solely to maternal analgesic drugs is rare and should not occur at all under prompt and proper anesthesiologic management even without the use of Nalline.* This opinion is based on an extensive personal experience with obstetric anesthesia.[8, 19]

Since general anesthesia should be avoided when Nalline is most needed, the obstetrician might be tempted to reduce the need for expert anesthesiologic service (in some institutions this is already true). On the contrary, the liberal administration of narcotic analgesia, with or without the use of Nalline, imposes a greater burden on the anesthesiologic service, and also multiplies the duties of personnel in the delivery room and nursery and adds an element of uncertainty and concern to the early neonatal course. In my own obstetric anesthesiologic services, the narcotized parturients and newborn infants, delivered by obstetricians who depend on Nalline, usually require more energetic and prolonged care. This is especially true when the obstetrican insists on the use of general anesthesia and avoids conduction methods for the delivery. When Nalline passes out of the hands of special investigators and high anesthesiologic standards are not observed in obstetric service, the evils of narcotic obstetric analgesia will again be experienced by a new generation of patients and obstetricians, despite the use of Nalline.

Summary and Conclusions

The routine use of nalorphine in the parturient, either with each dose of narcotic or 10 to 20 minutes before delivery, is unjustified because (1) only a small minority of narcotized mothers give birth to depressed infants, (2) in the absence of general anesthesia the incidence and management or neonatal asphyxia is not significantly improved by nalorphine, (3) in the presence of general anesthesia the benefit of nalorphine is not evident; it tends to prolong maternal depression, and after ether to aggravate neonatal depression.

On the basis of present evidence the most practical and effective method of administering nalorphine is by umbilical vein only when required. Neonatal depression can then be evaluated and its cause determined, if possible, before any drugs are injected. Nalorphine, although a mild depressant, can re-enforce the effect of other depressant factors or states. Nalorphine should be avoided when neonatal respiration and/or circulation are depressed primarily by causes other than narcotics.

The safety of the newborn after the liberal use of narcotic obstetric analgesia depends, first, on high quality of anesthesiologic care; second, on avoidance of general anesthesia; third, and only occasionally, on the proper administration of nalorphine by umbilical vein.

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PRENATAL FETAL ELECTROENCEPHALOGRAPHY

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THE problem of evaluation of the fetus in utero has heretofore been limited to determination of life or death. Slowing of the fetal heart rate has been given as an indication of intrauterine fetal distress as have other less tangible factors. Fetal electrocardiography and phonocardiography have been employed to determine intrauterine fetal distress before it becomes clinically evident, but have failed. They will record changes in rate and occasionally in rhythm of the fetal heart and detect fetal heart murmurs. All these aberrations are usually apparent by simple auscultation. They give no forewarning of fetal difficulty. The search for a more accurate procedure which would reflect the status of the fetus in utero was initiated.

It was believed that recording of the electrical activity of the brain of the fetus in utero might prove to be such a sensitive procedure. Lindsley[1] had previously reported the similarity of tracings from the lower abdomen of a pregnant woman (last trimester) to those obtained directly from the skull of a newborn infant.

Okomoto and Kirikae[2, 3] employed direct electroencephalography (needles in fetal brain) to record waves from fetuses which ranged in age from 3 to 9 months of gestation. The human fetuses were obtained from abdominal or vaginal termination of the pregnancies. The recordings showed very irregular waves of 10 to 90 microvolts with the superimposition of regular fast waves of 5 microvolts.

Borkowski and Bernstine[4] studied two fetuses of less than 3 months of age. Their results were extensively reported elsewhere, but in the main show high-voltage slow-wave activity with superimposed small fast waves. In one case tracings were taken from the surface of the extirpated uterus and showed low voltage activity at 2 per second.

Various investigators have reported on the electroencephalogram of the newborn infant. Sureau, Fischgold, and Capdevielle[5, 6, 7] found the fundamental frequency to be very slow (1 to 3 cycles per second, but very rapid frequencies were clearly visible superimposed on these slow waves.

In the present series, recordings were taken directly from the skull of the newborn within a short time after delivery (usually within one hour) and in all instances the tracings obtained were almost identical with the prenatal uterine tracing (Fig. 5).

In the one instance of intrauterine fetal death no waves as described previously were obtained.

Procedure

The recording of the electroencephalogram of the fetus in utero was attempted by use of abdominal and vaginal leads. The patient was instructed to void prior to the test. She was allowed to assume a comfortable semi-reclining position. Electroencephalogram electrodes (Grass) were placed on the abdomen as indicated in Fig. 1. When vaginal leads were employed, a specially constructed vaginal Lucite mold with solid silver electrodes was used (Fig. 2). The electrodes were placed in the mold at 9, 12, 3, and 6 o'clock.

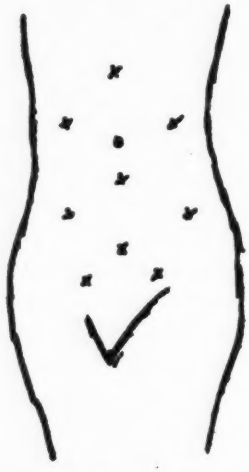


Fig. 1.—Represents position of abdominal electrodes.

The Lucite mold is inserted into the vagina under the usual sterile conditions observed in doing a vaginal examination on a pregnant woman at or near term. The silver electrodes are then slowly advanced beyond the extent of the mold. Because of their sites of exit from the mold, and their inherent flexibility, the electrodes will find their way to each of the fornices above the level of the cervix. A definite resistance is met at this stage of their insertion. All recordings were taken on a standard 8-lead electroencephalogram machine. All readings were bipolar.

Results

Abdominal.—The summary of the patients tested and results obtained are presented in Table I. In 18 of 20 patients tested, activity was observed which we feel represents the electroencephalogram of the fetus in utero. In one instance there was questionable activity. All infants were born alive.

The fetal electroencephalogram showed slow waves of ½ to 2 per second of low voltage; occasionally faster waves (6 to 12 per second) of low voltage were observed; and in one instance very fast activity (22 per second) of low voltage was seen.

The electrodes applied to the maternal abdomen in close proximity to the fetal head demonstrated this activity (Fig. 4).

Vaginal.—The summary of the patients (12) tested and the results obtained are presented in Table II. In all instances except two, a fetal electroencephalogram was obtained. In one instance the cooperation of the patient was not

obtained and the test was terminated prematurely after considerable movement of the patient. In the other patient the fetus was born dead one week after the test. The mother had not felt any fetal movement for several days and it was the clinical impression of the house staff that this represented a case of intrauterine fetal death.

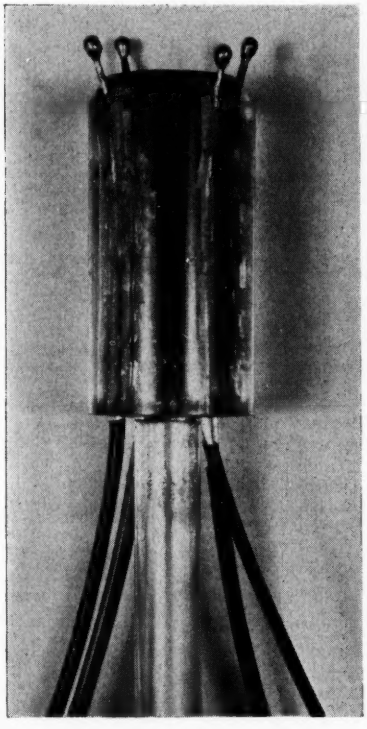


Fig. 2.—Lucite vaginal mold with silver electrode wires.

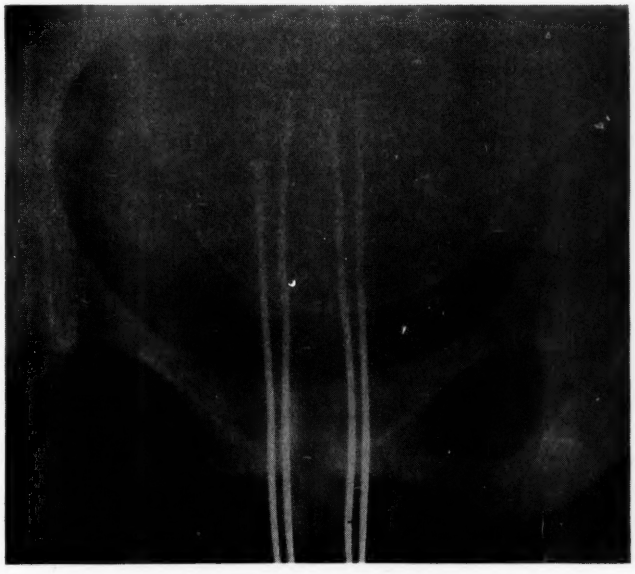
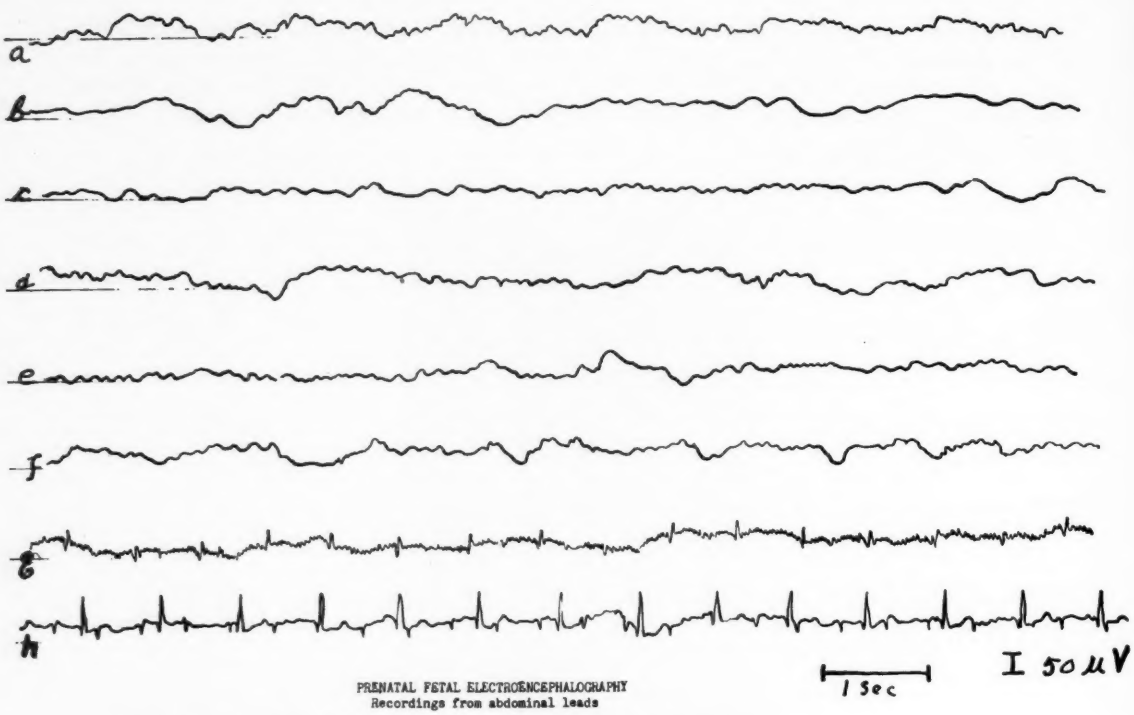


Fig. 3.—Roentgenogram of vaginal mold in place.



PRENATAL FETAL ELECTROENCEPHALOGRAPHY
Recordings from abdominal leads

a. (JH) slow waves at 1/2 to 2 per sec. with superimposed waves at 12 per sec.
b. (RML) slow waves at 1 per sec. with superimposed waves at 5 per sec.
c. (MCM) slow waves at 1/2 to 2 per sec. superimposed waves at 12 per sec.
d. (DA) slow waves at 1 per sec. with superimposed waves at 7 per sec.
e. (RML) slow waves at 2 per sec. with superimposed waves at 12 per sec.
f. (PJ) slow waves at 2 per sec. with superimposed waves at 8 per sec.
g. (FF) fast waves at 22 per sec.
h. fetal electrocardiogram

Fig. 4.—Tracings obtained off the maternal abdomen from electrodes in proximity to the fetal head.

The fetal electroencephalogram consisted of slow waves (3 per second) of low voltage (10 to 20 microvolts); in three instances very fast activity (18 to 24 per second) of low voltage was seen.

Hyperventilation of the mother for three minutes produced a slight build-up of activity in four cases. No untoward results occurred as a result of this procedure.

Comment

The differentiation of the recorded activity from the various other possible sources does not offer great difficulty in most instances. The artifacts produced by uterine contractions of labor are sharp bursts of high voltage activity which may be correlated with the patient's knowledge of a "labor pain." The rhythmic contractions of the uterus during pregnancy and prior to labor are slow and of high voltage and occur chiefly in the fundal area rather than in the lower segment. Steer and Hertsch[8] found practically no uterine activity in the lower portion of the uterus.

We feel that the activity presented represents the fetal electroencephalogram for the following reasons: (1) The same activity has been recorded directly from the brain of newborns and fetuses by Okomoto and Kirikae[2, 3] and Borkowski and Bernstine.[4] (2) In several instances the vaginal electrodes were

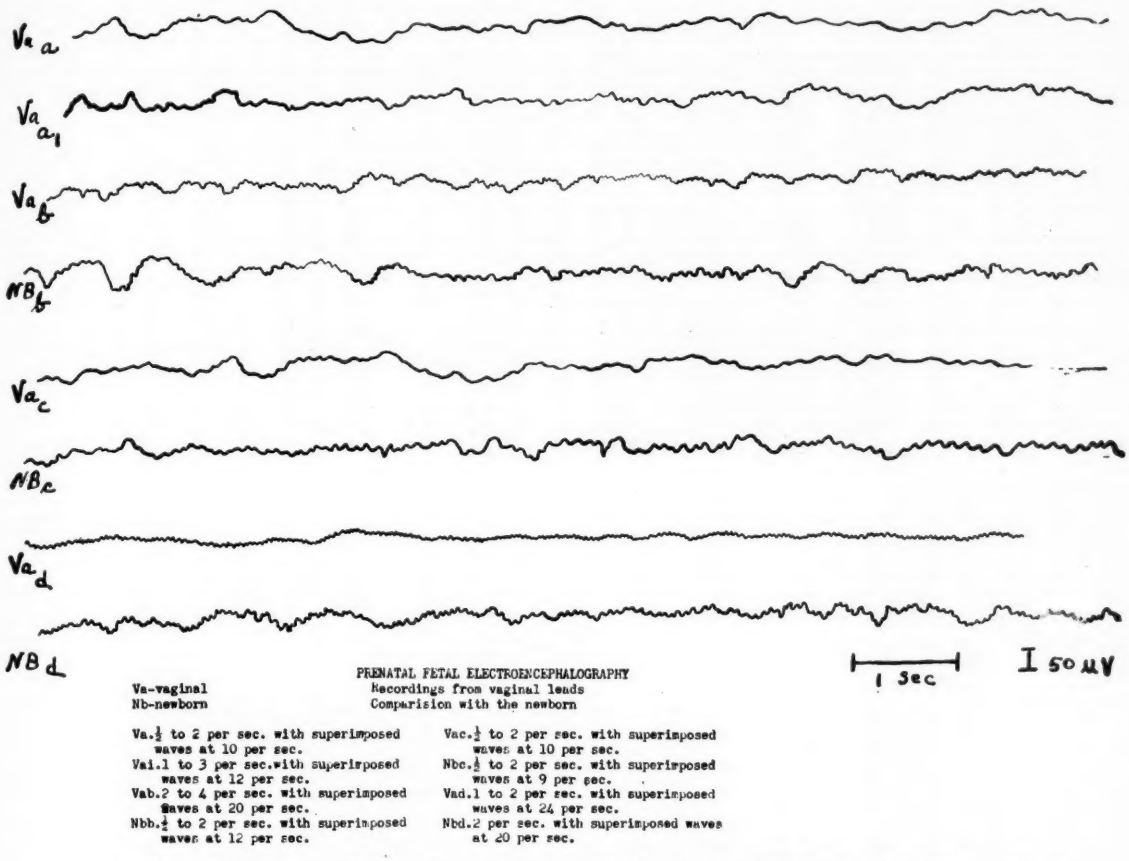


Fig. 5.—Comparison of tracings from vaginal electrodes and directly from skull of newborn infant (within 6 hours after delivery).

directly against the fetal skull during the recording. (3) The activity recorded from the abdominal electrodes was recorded only from those electrodes in close proximity to the fetal skull. (4) Close correlation in individual cases was noted between prenatal tracings and those obtained from the skull of the newborn immediately after delivery. (5) Activity in one fetus was recorded from the surface of the excised uterus, then from the intact amniotic sac, and from the surface of the fetal skull, and finally from the brain, itself. The type of activity bears close resemblance to that recorded from the pregnant maternal abdomen in the vicinity of the fetal skull and from the vagina.

Summary

1. Two methods (abdominal, vaginal) of demonstrating the electroencephalogram of the fetus in utero are presented.

2. Positive results were obtained in 87 per cent of 32 patients tested.

3. Comparison is made of the tracings obtained from the maternal abdomen in proximity to the fetal head and from the vagina with the tracings obtained directly from the brains of fetuses and the skulls of newborn infants. The close similarity is noted.

TABLE I. SUMMARY OF PATIENTS TESTED (ABDOMINAL)

PATIENT	AGE	RACE	GRAVIDA	PARA	WEEKS OF PREGNANCY	COMPLICATIONS OF PREGNANCY	CONDITION OF BABY (BIRTH)	RESULTS
A. McC.	30	N	vii	vi	40	Essential hypertension	Good	Low-voltage slow waves at 3 per sec. Build-up of activity with hyperventilation
W. M. McD.	30	N	x	vi	40	Sickle-cell anemia Hypertension	Good	Low-voltage slow waves at 3 per sec. Mild build-up of activity with hyperventilation
M. T.	20	N	iv	iii	40	Epilepsy	Good	Low-voltage slow waves at 3 per sec. with superimposed fast waves at 22 per sec.
F. C.	29	W	iii	ii	36	None	Good	Low-voltage slow waves at 3 per sec. with superimposed fast waves at 20 per sec. Build-up of activity with hyperventilation
F. C.	29	W	iii	ii	40	None		Low-voltage slow waves at 3 per sec.
L. M. F.	33	N	iv	iii	36	None	Good	Low-voltage slow waves at 3 per sec. Mild build-up of voltage with hyperventilation
J. C.	36	N	v	iv	40	Severe pre-eclampsia Triplets	Good	Low-voltage slow waves at 3 per sec.
M. E. P.	21	W	i	0	36	Hypertension	Good	Low-voltage slow waves at 3 per sec.
B. K.	20	N	iv	ii	44	Essential hypertension	Good	Low-voltage slow waves at 3 per sec. with superimposed fast waves at 20 per sec.
R. McC.	30	N	v	iv	40	Essential hypertension	Good	None observed
R. N.	24	W	v	iii	40	None	Good	Low-voltage slow waves at 3 per sec.
S. E.	35	N	iii	ii	22	Intrauterine fetal death	Stillbirth	None observed

TABLE II. SUMMARY OF PATIENTS TESTED (VAGINAL)

PATIENT	AGE	RACE	GRAVIDA	PARA	WEEKS OF PREGNANCY	COMPLICATIONS OF PREGNANCY	CONDITION OF BABY (BIRTH)	RESULTS
F. G.	23	N	iv	iii	40	None	Good	Low-voltage slow waves at 2 per sec.
D. K.	22	N	i	0	26	Pre-eclampsia	Good	None observed
B. L. M.	28	W	i	0	43	Rheumatic heart disease (inactive)	Good	Low voltage at 7 to 10 per sec.
E. C.	41	W	iii	ii	33	Twins Pre-eclampsia	Good	Low-voltage slow waves at 5 per sec.
J. G.	19	N	ii	i	32	None	Good	Low-voltage waves at 6 to 12 per sec.
J. H.	26	N	iii	ii	35	Sickle-cell anemia	Good	Low-voltage slow waves at ½ to 2 per sec. with superimposed waves at 6 to 12 per sec.
R. L. S.	35	N	ix	viii	40	Pre-eclampsia	Good	Low-voltage waves at 12 per sec.
M. C. M.	37	W	vi	v	40	None	Good	Low-voltage slow waves at ½ to 2 per sec. with superimposed waves at 12 per sec.
A. R.	21	W	iii	ii	33	None	Good	Low-voltage slow waves at ½ per sec. with superimposed waves at 12 per sec.
P. M. C.	22	N	iv	iii	32	None	Good	Low-voltage slow waves at 2 per sec.
J. T.	17	N	i	0	32	None	Good	Low-voltage slow waves at 2 per sec.
D. H.	21	N	iii	ii	32	Sickle-cell anemia	Good	Low-voltage slow waves at 2 per sec.
R. M. L.	36	W	vi	v	33	None	Good	Low-voltage slow waves at 2 per sec. with superimposed waves at 12 per sec.
R. M. L.	36	W	vi	v	36	None	Good	Low-voltage slow waves at 1 per sec. with superimposed waves at 5 per sec.
C. K.	38	W	vi	v	37	Hypertension (mild)	Good	Questionable
D. A.	24	N	iv	iii	30	Pre-eclampsia	Good	Low-voltage slow waves at 1 per sec. with superimposed waves at 7 to 12 per sec.
P. J.	26	N	ix	viii	38	None	Good	Low-voltage slow waves at 2 per sec. with superimposed waves at 8 per sec.
E. A.	18	W	i	0	32	None	Good	Low-voltage slow waves at 1 per sec. with superimposed waves at 6 per sec.
N. L. W.	22	N	i	0	38	None	Poor at birth; responded to resuscitation	Low-voltage slow waves at 2 per sec.
F. F.	17	W	i	0	38	Pre-eclampsia		Low-voltage fast waves at 22 per sec.

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PRENATAL FETAL ELECTROCARDIOGRAPHY

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THE evaluation of the fetus in utero has depended on auscultation of fetal heart sounds for many years. In 1906 Cremer[1] noted small deflections, apparently due to the fetal heart action, while recording the electrocardiogram of a pregnant woman at term. Since that time sporadic attempts have been made to develop and refine the technique of fetal electrocardiography. The standard electrocardiogram machine has been replaced by more sensitive apparatus. The limb leads have been superseded in most instances by abdominal leads. Rectal, vaginal, cervical, and intrauterine application of electrodes has been tried. Constant positive results are obtainable in almost 100 per cent of cases in the last trimester of pregnancy, and even in early pregnancy the results are encouraging; nevertheless, this procedure has not found widespread use in the United States. It was believed of value to review the previous literature (Table I) on this subject and to present our experiences with fetal electrocardiography.

The fetal heart apparently possesses electrical activity at a very early age. The exact stage of development in human fetuses in which this activity is present is yet to be determined. Theoretically, electrocardiographic tracings should be obtainable at the 16 to 30 somite stage (25 to 30 days) when the fusion of the primitive heart tubes occurs.

Patten,[47] studying chick embryo hearts, demonstrated an adult-type electrocardiogram before the sinoventricular conduction system is present, before accelerator or depressor nerves reach the heart, and before the coronary circulation is established.

Borkowski and Bernstine[55] demonstrated the incidental finding of an electrocardiogram from a 42-day-old human fetus (16 mm.). Goodyer[19] obtained an electrocardiogram from an 18 mm. fetus using head and rump leads.

Apparatus

The instrument used in this study was the standard 8-lead Grass electroencephalogram machine. The electrodes were standard EEG electrodes and were applied to the mother with the use of electrode paste.* The standardization was 50 millivolts to equal 1 mm. deflection. Greater amplification did not improve the results.

*Soak 85 Gm. 200 mesh bentonite in 385 ml. water overnight. To 350 Gm. of this paste add a solution of 80 Gm. calcium chloride dissolved in 60 ml. water. Mix result with 30 ml. glycerine.[53]

TABLE I. SUMMARY OF PREVIOUS STUDIES ON FETAL ELECTROCARDIOGRAPHY

REF. NO.	AUTHOR	DATE	NO. OF CASES	PERIOD OF GESTATION	LEADS	RESULTS	INSTRUMENT
1.	Cremer	1906	1	Term	Extremities	Positive	String galvanometer
2.	Foa	1911	1	8½ months	Abdomen-vagina	Positive	String galvanometer
3.	Krumbhaar	1916	1	Term	Abdomen	Positive	String galvanometer
4.	Sachs	1922	Not stated	Term	Abdomen-vagina Abdomen-rectum	Negative	String galvanometer
5.	Haynal Kellner	1924	Not stated	Not stated	Abdomen	Not stated	String galvanometer
6.	Maekawa Toyoshima	1930	1	Term	Abdomen	Positive	String galvanometer Valve amplifier
7.	Steffan Strassmann	1933	1	Past term	Abdomen Extremities	Positive	Standard ECG
8.	Strassmann	1936	1	Term	Extremities	Positive	Tension ECG
9.	Johnson	1938	1	Term	Extremities	Positive	Standard ECG
10.	Bell	1938	35	Last 2 months; 2 cases, 5½, 6 months	Abdomen Rectum Lower back	28%	Thermionic Valve ECG
11.	Strassmann Mussey	1938	70	Term Last 70 days	Extremities	87%	Standard ECG
12.	Burnham	1939	1	7 months	Abdomen	Negative	Not stated
13.	Strassmann	1939	70	Term	Extremities	87%	Standard ECG
14.	Dressler Moskowitz	1941	40	Last 67 days	Extremities	80%	Standard ECG
15.	Monroe	1941	17	Last 70 days	Abdomen	76%	Standard ECG Pre-amplifier
16.	Geiger Monroe Goodyer	1941	Not stated	Fourth month to term	Abdomen	Not stated	Standard ECG Single-stage resistance couple amplifier
17.	Mann Bernstein	1941	76	Fourth month to term	Extremities Abdomen	74%	Standard ECG Amplifier
18.	Putz Ulrich	1941	35	Term One in sixth month	Abdomen	Not stated	Standard ECG
19.	Goodyer	1942	124	17 weeks to term	Abdomen	84%	Standard ECG Preamplifier EEG
20.	Goodyer Geiger Monroe	1942	181	Fourth month to term	Abdomen Vagina	87%	Standard ECG Preamplifier
21.	Lindsley	1942	3	Fifth, seventh, eighth months	Abdomen	100%	Oscillograph Amplifier
22.	Bernstein Mann	1942	99	3 months to term	Abdomen	75%	Standard ECG Amplifier

TABLE I—CONT'D

REF. NO.	AUTHOR	DATE	NO. OF CASES	PERIOD OF GESTATION	LEADS	RESULTS	INSTRUMENT
23.	Ward Kennedy	1942	46 38	Fourth month to term	Abdomen	67% 82%	Crystograph Amplifier
24.	Tarnower Lattin	1942	2	Eighth month	Not stated	Negative	Not stated
25.	Sondergaard	1942	56	4 months to term	Abdomen	90%	Standard ECG Amplifier
26.	Putz Ulrich	1942	43	Term	Abdomen	86%	Standard ECG Amplifier
27.	Mann Mayer	1942	1	Term	Abdomen Uterus Fetus directly	Positive	Not stated
28.	Borter	1943	433	Term	Rectum Abdomen	100%	Standard ECG Intensifier
29.	Paley Krell	1944	21	Seventh month to term	Abdomen Extremities	53%	String galvanometer Amplifier
30.	Bedoya Frade	1945	12	Seventh month to term	Abdomen Lower back	66%	Standard ECG Amplifier
31.	Plant Steven	1945	1	Eighth month	Abdomen	Positive	Standard ECG Amplifier
32.	Hedberg	1945	1	Term	Not stated	Negative	Not stated
33.	Vara Halmiven	1946	30	3 months to term	Abdomen Vagina Intrauterine	100%	Standard ECG Amplifier
34.	Alimurung	1947	1	In labor	Extremities	Positive	Standard ECG Amplifier
35.	Blondheim	1947	28	Last 5 months	Abdomen	82%	EEG
36.	Pfister Plice	1950	36	Term Two at mid-pregnancy	Abdomen Extremities	100%	Standard ECG Amplifier
37.	Putz Rommelspacker Wolff	1950	7	Term	Abdomen	86%	EEG
38.	Nyman	1951	32	2 to 6 months	Abdomen Vagina Cervix	62%	Standard ECG Amplifier
39.	Vara Niemineva	1951	4	11, 15, 18, 19 weeks	Abdomen Uterus Fetus directly	100%	Not stated
40.	Smyth	1953	100+	Not stated	Abdomen Vagina Rectum Intrauterine	100%	Standard ECG Amplifier
41.	Wimmer	1954	180 150	Seventeenth week to term	Abdomen	78% 94%	Standard ECG 25 mm./mv. Amplifier 100 mm./mv.
42.	Southern	1954	190	Seventeenth week to term	Abdomen	85%	Standard ECG Amplifier

Various investigators have used different apparatus from the string galvanometer to special amplifier system attachments to the standard electrocardiogram. In general, some degree of amplification over the standard electrocardiogram machine is necessary to obtain constant results. As the machine used varies with individual reporters, so do the electrodes used. Specially constructed electrodes have been utilized in addition to the standard electrocardiogram or electroencephalogram electrodes. It is questionable whether these electrodes improve the results.

Method

In general, positioning of the patient was such as to provide maximum relaxation of the abdominal musculature. The mother was allowed to assume a reclining position, but patients who were faint or dyspneic in this position were allowed to sit, leaning slightly forward. The bladder was emptied immediately prior to the test. The patient was reassured and the test was briefly explained to her. The electrodes were placed on the abdomen utilizing chiefly the midline (linea alba) and the immediate suprapubic area. When the patient was tested in the sitting position, electrodes were placed in addition on the lower back, especially in the region of the lumbosacral junction.

Vaginal leads were tried in many cases but they yield results inferior to abdominal leads and require special equipment and technique of insertion. Their usage in early pregnancy is of apparent value (Nyman[38]). Rectal leads are painful to the patient and are not necessary.

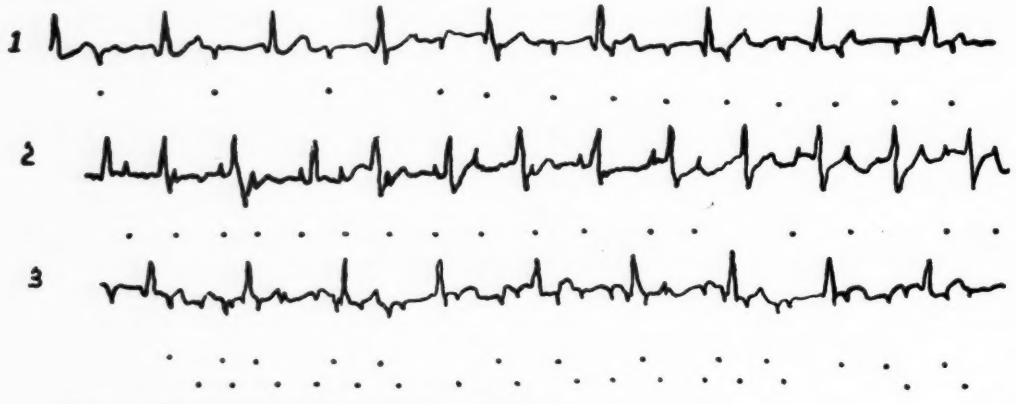

Fig. 1.—Examples of fetal electrocardiograms.*
1, Tracing of a single fetus—head presentation.
2, Tracing of a single fetus—breech presentation.
3, Tracing of a twin pregnancy—both presenting as vertexes.

Interpretation of Tracings

As one gains experience with this procedure, the various artifacts which may distort the tracing do not offer great difficulty. Improvement in technique will cause many to disappear.

Dressler and Moskowitz[14] suggest the following criteria for considering a fetal electrocardiogram as positive: (1) the R wave must be followed throughout the entire lead; (2) it must occur at fairly regular time intervals; (3) the fetal electrocardiogram should be correlated with phonocardiograph of the fetal heart. We do not believe the third feature is necessary and it provides a cumbersome addition to the procedure.

*Dots indicate fetal cardiac complexes.

The regularity and rate of the typical fetal electrocardiogram offer no difficulty in detection.

In the present series no attempt is made to analyze the results from its relation to the size of the fetus, amount of amniotic fluid or amount of vernix caseosa, and fetal maturity. Goodyer,[19] and Wimmer,[41] have provided extensive remarks on these subjects. Goodyer in a series of 124 electrocardiograms was unable to find any correlation with fetal size and size of the electrocardiogram. The decrease in the percentage of positive tracings in the seventh and eighth months of gestation was previously attributed to a relative increase in the amount of amniotic fluid. With more sensitive methods this period of pregnancy is no longer unique in this respect. Wimmer correlated the smaller size of the fetal waves to a larger amount of vernix. He was able to demonstrate an increase in the size of the fetal wave with the infant who was clinically postmature and possessed little or no vernix. Our preliminary observations tend to confirm Wimmer's findings.

Results

Fetal electrocardiograms was taken on 50 patients. In all instances of a living fetus a positive tracing was obtained. Two cases of intrauterine fetal death, two sets of twins, and one set of triplets are included in the present series. All tests except one were performed on patients in the last half of pregnancy.

Practical Considerations

The value of fetal electrocardiography lies in the diagnosis of fetal existence. It does not determine anoxia or distress except perhaps indirectly by change in rate of the fetal heart.

1. The Evidence of Fetal Life.—

In late pregnancy with an experienced observer in this procedure the absence of the fetal electrocardiogram definitely indicates the death of the fetus in utero. A positive tracing offers undeniable evidence of fetal life.

The obese or polyhydramnic patient frequently presents a problem in eliciting fetal heart tones. The use of the electrocardiogram circumvents this obstacle.

Bieber[49] reports a series of 353 cases of premature separation of the placenta in 23.3 per cent of which no fetal sounds were heard but live infants were born. He did not make use of fetal electrocardiography, but the fertile field for application of this test is at once evident.

The usual hormonal tests for pregnancy reflect functioning chorionic tissue. They do not directly indicate fetal life. The titer of chorionic gonadotrophin may persist at a high level for a week after intrauterine death, or even much longer.

The endocrine laboratory at Jefferson Medical College Hospital has on record several cases of titers of chorionic gonadotrophin as low as 200 rat ovary hyperemia units in late pregnancy with the subsequent birth of a living healthy infant.[54]

The differentiation between hydatidiform mole and normal pregnancy may be determined when a positive electrocardiographic tracing is obtained. The same reasoning applies in suspected cases of abdominal tumors which simulate pregnancy.

The results are obtained immediately and require a minimum of interpretation.

The use of fetal electrocardiography in early pregnancy is limited and the positive results obtained are fewer. Nyman[38] has applied combined abdominal

and intracervical leads in pregnancies as early as 54 days after a missed menstrual period. These are cases in which interruption of the pregnancy was deemed necessary. If Nyman demonstrated a fetal electrocardiogram, surgical interruption was performed. The value of the procedure requires further investigation. We have not had any success in using vaginal leads in either early or late pregnancy. The application of this procedure in suspected cases of ectopic pregnancy may yield interesting results.

The following two cases are illustrative.

CASE 1.—Mrs. E. A. was a primigravidous patient in the seventh month of pregnancy who had had vaginal spotting for two days prior to admission. No fetal movement had been present for a similar period of time; it was not possible to elicit fetal heart tones. The fetal electrocardiogram showed definite fetal spikes. A living infant was born at term.

CASE 2.—Mrs. R. S., a multigravidous patient in the third month of pregnancy, had been treated for threatened abortion and responded well. A fetal electrocardiogram demonstrated definite fetal spikes. Pregnancy progressed satisfactorily.

2. Presentation.—

The presentation, cephalic or podalic, can be accurately diagnosed by the direction of the fetal wave. The fetal wave is in the same direction as the mother's in cases of breech presentation (provided the readings are taken from cephalad to caudad on the maternal abdomen). In cases of oblique or transverse lie, the position of the fetus may be determined by taking several readings about the fetal ovoid and comparing the size and direction of the fetal waves.

3. Multiple Pregnancies.—

The value of fetal electrocardiography in diagnosing multiple pregnancies is limited. With the definite evidence offered by roentgenograms and the possibility of overlooking the extra set or sets of deflections, the test should not be expected to give dependable results in this field. The theoretical application of the test in early pregnancy when x-ray may not be desirable or may not yield conclusive results awaits future perfection in technique.

4. Fetal Heart Aberrations.—

Sporadic reports are available on the occurrence of intrauterine fetal tachycardia and arrhythmias in utero. In most instances no accompanying electrocardiogram was taken. The intrauterine diagnosis of fetal heart anomalies is not now possible. The accomplishment of this phase of fetal electrocardiography lies in the development of a technique which will demonstrate P waves. Nevertheless, the presence of an abnormal fetal heart rate will alert the obstetrician and cardiologist to expect an infant who on delivery will require diagnostic procedures and may require immediate treatment to sustain extrauterine life.

Hyman[50] (using electrocardiogram and phonocardiogram) classifies intrauterine fetal cardiac irregularities as follows: (a) exaggerated physiologic disturbance of the pacemaker producing sinus arrhythmia (responsible for 80 per cent of irregularities); (b) skipping or alteration in regular rhythm of heart (possibly due to intrauterine extrasystoles); and (c) grossly abnormal fetal heart rhythms.

He encountered fetal cardiac irregularities in 9.2 per cent of the cases studied.

We have been interested in the effect on the fetus of administering cardiac drugs (digitalis, quinidine, etc.) to pregnant women. In two instances, we have not been able to show any effect of these drugs on the fetus in utero or immediately after delivery. Both infants were normal in all respects.

Comment

The earlier work with fetal electrocardiography was limited by the sensitivity of the apparatus. Within recent years development of various amplifying systems and the use of the electroencephalogram machine has provided the added degree of sensitivity which makes the test a useful clinical adjunct.

The applicability of fetal electrocardiography to the later months of gestation is acknowledged by the consistently positive results obtained in instances of living fetuses. Although the test shows evidence of value in early pregnancy, the technique requires further refinement to meet the criteria of a clinically useful test. The theoretical minimum stage at which the electrocardiogram can be obtained is as early as the 16 to 30 somite stage (25 to 30 days) when fusion of the primitive heart tube occurs in the human embryo. Heart tracings have been obtained directly from very early fetuses.

The applicability of fetal electrocardiography to determining fetal maturity and assessing fetal anoxia is yet to be fully determined. The manifold prospects of this technique are not yet completely explored.

Summary

1. A complete review of the literature on fetal electrocardiography to date is presented.

2. A simple technique is presented which is especially applicable in late pregnancy.

3. Fifty consecutive cases are presented in which positive tracings were obtained in all instances of a living fetus.

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PLACENTAL TRANSMISSION OF THIOPENTAL*

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IN 1944, Hellman and associates[1] published a report on the use of thiopental (Pentothal sodium) combined with nitrous oxide for terminal anesthesia in 1,415 obstetrical cases. In 7 of their cases maternal venous blood and mixed umbilical cord blood were analyzed to determine the thiopental concentrations present in the mother and infant at the time of delivery. They concluded that there was a period of five minutes after the initial injection during which the amount of drug reaching the infant was extremely small, and that an equilibrium between the maternal and fetal blood thiopental concentrations was not reached until eight to twelve minutes after the initial injection.

On the basis of this work several reports have appeared in the literature advocating the use of thiopental for cesarean sections and vaginal deliveries.[2-6] Each recommends that the infant be delivered within eight to twelve minutes following injection of the drug.

Gustafson and Gardner[7] were unable to correlate clinically the condition of the baby immediately following delivery with the total dosage of thiopental administered to the mother, nor with the time interval between the initial injection of the drug and the delivery of the infant. A similar lack of correlation between the total dose of thiopental and the fetal respiratory response following delivery has also been reported by Pavey[8] and Whyte.[9] Whyte[9] states, "Our experience indicates that the dangers to the infant due to narcotic concentrations accumulating in the blood have been overemphasized. We feel that concentrations sufficient to maintain satisfactory maternal anesthesia may be safely employed for considerably longer than the previously recommended time." No blood studies to determine the thiopental concentrations were carried out in these cases nor was the amount of drug and the time interval between the last injection and delivery related to the fetal respiratory response following the delivery.

Clinical observation and studies by Bollman and co-workers[10] and Brodie and associates[11] have indicated that thiopental is transmitted from the blood stream to the tissues of an individual in less than one minute. The present study was undertaken to determine whether a specific placental barrier exists to thiopental to account for the relatively low cord concentrations reported, or whether thiopental diffuses into the cord blood in less than the generally accepted time.

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Method

Fifteen normal obstetrical patients at term were studied during their deliveries. The patients' ages ranged from 20 to 41 years. Six patients were delivered spontaneously, 6 required low forceps extractions, and three were subjected to repeat cesarean sections. No patient was included in the study if there had been any difficulties during the prenatal period or the labor, or if the infant was thought to be premature, abnormal, or in an unusual position.

The 12 patients delivered vaginally received premedication of 75 to 100 mg. Demerol hydrochloride and 0.4 to 0.6 mg. scopolamine hydrobromide from one-half to four hours prior to delivery. At delivery, anesthesia was established with nitrous oxide-oxygen delivered in a 75-25 per cent concentration, except for one instance in which ether was added to the anesthetic mixture. The three patients subjected to cesarean section had premedication of 0.6 mg. of atropine sulfate or scopolamine hydrobromide an hour and one-half prior to the induction of spinal anesthesia with 8 mg. Pontocaine hydrochloride.

When delivery of the infant was deemed imminent a single standard dose of 350 mg. of a 5 per cent solution of thiopental was injected into one of the antecubital veins of the mother and the time recorded. The delivery was completed, and as soon as possible the umbilical cord was clamped. A 5 c.c. sample of blood was collected from the fetal segment.* Coincidentally with the clamping of the cord a tourniquet was applied about the mother's arm opposite to that used for the thiopental injection and a 5 c.c. sample of venous blood was drawn. The samples of maternal venous blood and mixed cord blood were analyzed for thiopental within eight hours, by the ultraviolet absorption method described by Brodie and collaborators.[11]

TABLE I. MATERNAL AND INFANT BLOOD LEVELS OF PENTOTHAL

CASE NO.	TIME (MINUTES)	BLOOD LEVELS (MG. %)		REMARKS
		MATERNAL	FETAL	
2	0¾	3.450	0.800	Infant depressed
8	1¼	2.26	0.185	
12	1¼	3.02	0.332	
14	1½	1.83	0.225	
16	2	1.83	1.32	Cesarean section
10	2	2.62	1.69	
6	2¼	1.70	1.43	Infant depressed
1	2½	1.52	3.10	? Lab. Error
17	2¾	1.25	2.56	? Lab. Error
9	3	2.67	1.185	Cesarean section
18	3	1.84	1.88	Infant depressed
19	3	1.31	1.31	
3	3¾	1.08	1.34	
11	5	1.13	1.20	
5	7½	0.657	0.775	Cesarean section

Laboratory accuracy determined ± 10 per cent.

Results

Thiopental concentrations found immediately following the delivery of the infants in the mixed umbilical cord blood and in the venous blood of the mothers are listed in Table I. In the mothers, the shorter the interval between the injection of thiopental and the blood sampling, the higher was the blood thiopental concentration, especially during the first few minutes. Since blood volume or body mass determinations were not made, quantitative comparisons

*It was considered that any change in the thiopental concentration in the cord blood occurring between application of a clamp and obtaining a sample of blood would be negligible.

between the thiopental concentrations of the mothers are not possible. This study was intended only to compare the thiopental concentration of the mother and her child at varying times following a single injection of the drug.

It is evident also that there was an early appearance of thiopental in the mixed cord blood of the infant. During the three-minute interval after the administration of the drug to the mother the cord concentration rose rapidly. An approximate equilibrium between the cord blood and the mother's venous blood appeared to be reached in about three minutes.

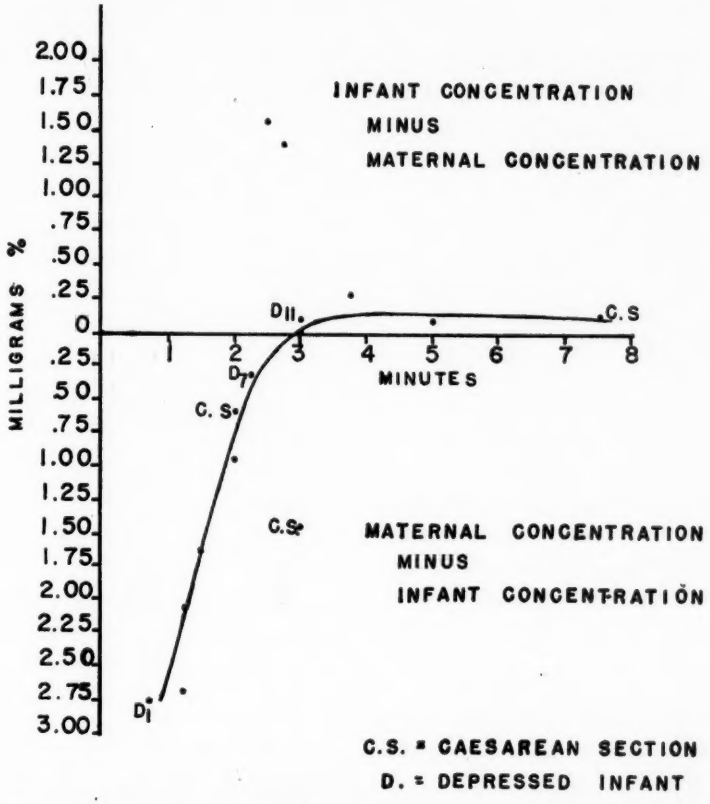

Fig. 1.—The difference in thiopental concentrations of mixed cord blood and maternal venous blood in 15 cases. Zero (0) line represents equal concentrations in fetal cord blood and maternal blood. Further explanation is in the text.

Fig. 1 represents the difference between maternal and fetal blood thiopental concentrations plotted against the time interval between the injection of the drug to the mother and the blood sampling immediately after delivery. Zero (0) line on the graph indicates equal concentrations of thiopental in the mixed cord blood and in the maternal venous blood, i.e., equilibrium between infant and mother. Below this line, the concentration is greater in the mother than in the infant; above the line the infant's blood has the greater concentration. Although the concentration of thiopental appears to be higher in the infants than in the mothers if delivery is delayed more than three minutes, the difference is not great and lies within our technical error of ± 10 per cent. The two values in which the infant blood levels are 1.25 and 1.50 mg. per cent higher than the maternal levels probably represent laboratory error. The low infant value in one of the cesarean sections represents early interference with the placental blood supply to the infant. In this instance the placenta was situated on the anterior uterine wall, necessitating its removal prior to the actual delivery.

Comment

It has been well established that thiopental administered to normal patients crosses the blood-tissue barrier very rapidly.[10, 11] It has also been shown that radioactive sodium,[12] alloxan in rats,[13] and other drugs[14] appear in the cord blood in from one to two minutes following injection into the mother. Various drugs of the barbituric acid group have also been shown to cross the placenta readily in hypnotic as well as anesthetic doses.[15, 16] There seems little reason to believe that thiopental also should not cross the placental barrier rapidly and in direct relation to the circulating maternal concentration. The results of this study appear to indicate that it does, reaching an equilibrium, following a single injection, in approximately three minutes.

It is difficult to explain in the light of these findings the clinical observations reported by Gustafson and Gardner,[7] Pavey,[8] and Whyte,[9] and confirmed by us, that the infants were not consistently depressed even when delivered close to the time when infant-maternal equilibrium was reached.

All but 3 of the infants in this series cried vigorously within three minutes of the delivery and many even before the body was delivered. The first depressed infant (D_1 in Fig. 1) was delivered from a mother who had received ether as well as nitrous oxide for about ten minutes prior to the delivery, and although the infant coughed four minutes following the delivery a good cry was not established for an additional six minutes. It is not felt that the concentration of thiopental (0.8 mg. per cent) in this case was responsible for its depressed state.

The second depressed infant (D_7 in Fig. 1) was delivered from a mother who had received 100 mg. Demerol two hours prior to the delivery. The infant cried vigorously after gentle oxygen resuscitation for 45 seconds. Why this infant was mildly depressed while others whose mothers received Demerol in similar dosage and time sequence were not, we cannot explain. The mixed cord blood thiopental concentration of this infant was not unusually high (1.43 mg. per cent), but nevertheless may have been a contributory, if not the major, cause of the depression.

The third depressed infant (D_{11} in Fig. 1) had the umbilical cord wrapped twice about his neck and required six minutes of artificial ventilation with oxygen before a cry was initiated. Although the depression was most likely due to hypoxia secondary to cord compression, it is interesting to note that the cord blood concentration of thiopental was the highest (1.88 mg. per cent) in the group and was essentially the same as the maternal blood concentration. At the time of delivery the two loops were slipped over the infant's head and circulation was re-established prior to clamping the cord. Diffusion of thiopental across the placental barrier into the trapped cord blood could have occurred even in the presence of cord compression. With the re-establishment of circulation it would have been carried to the infant before the cord was finally clamped. There would be no indication, however, of the length of time in which thiopental might have reached the infant, and it is difficult therefore to evaluate this case.

It is possible to explain the lack of correlation between the degree of depression of the infant with the thiopental concentrations of either mixed umbilical cord blood or maternal venous blood in several ways.

a. The infant liver, if it has the capacity to detoxify thiopental, may clear the blood more rapidly than the adult liver. Since a large portion of the cord arterialized blood passes through the infant's liver before general distribution, including distribution to the brain, it may be that a comparatively large quantity of thiopental must be passed through this organ before cerebral depression could occur.

b. Far more feasible is the probability that thiopental, like curare,[17] is distributed from the maternal blood stream to the maternal tissues so rapidly that the actual quantity of the drug reaching the infant is not enough to produce cerebral depression. Since it is the intracellular cerebral concentration of thiopental that is the determining factor in producing hypnosis rather than the blood concentration, unless the arteriovenous difference of thiopental in the umbilical cord, the time interval of transfer, and the rate of infant detoxification of thiopental are known, the concentration within the infant's brain cells cannot be estimated. Brodie and associates[18] have shown that thiopental is distributed in the body between a fat phase and a water phase, consisting of blood and organ tissues. They state, "Thiopental, administered intravenously, is rapidly distributed throughout the blood and organ tissue phase. Following this, the concentrations in blood and organ tissues decline as the anesthetic passes into fat." The tissue concentrations which they report tended to be higher than the plasma concentration. Theorizing, then, that a large proportion of the initial thiopental injection is removed from the mother's blood stream by her tissues, there may not be a great enough quantity of the drug transferred via the umbilical cord to permit concentrations within the infant's brain cells to reach a level adequate to produce infant depression. Under these conditions, the mother may be well anesthetized with thiopental alone, as in the cases reported by Whyte[9] and Pavey[8] or with thiopental and nitrous oxide as in the cases of Gustafson and Gardner[7] and in the cases of this series, and yet the infants show no evidence of depression at the time of delivery.

Over a longer period of time, if repeated injections of thiopental were relied upon for the maintenance of anesthesia, a greater percentage of each succeeding injection would reach the infant as the maternal tissues approached saturation levels, and narcotization of the infant would result. If one is to evaluate a series of patients delivered with thiopental anesthesia it is important to know not only the total amount of the drug administered over a period of time, but also the amount and time relationship of the last injection prior to the delivery.

It is our feeling that thiopental has a restricted place in obstetrics. For vaginal deliveries we feel that it should be administered only in a single, minimal injection in the last few minutes prior to the infant's birth. It should not be used as the primary anesthetic agent if there is any possibility that the delivery

might be prolonged. For cesarean sections, thiopental should be limited to the induction period only, and some other agent, in combination with curare if necessary,[19] should be used for the maintenance of anesthesia.

Summary

1. Thiopental administered to obstetrical patients immediately prior to delivery crossed the placental barrier rapidly, appearing in mixed fetal cord blood at least in 45 seconds and reaching an equilibrium with the maternal venous blood in three minutes.

2. With a few exceptions, infants delivered from mothers who had received thiopental were not depressed. No correlation between maternal depth of anesthesia, fetal responsiveness, and the thiopental concentrations of mixed umbilical cord and maternal venous blood was evident under the conditions of this study.

3. It is recommended that for vaginal deliveries thiopental be restricted to a single, minimal dose administered during the last few minutes of the delivery, and that for cesarean sections it be limited to the induction period.

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OBSERVATIONS ON PYRIDOXINE METABOLISM IN PREGNANCY

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DESPITE the rather frequent employment of pyridoxine in obstetrics and gynecology, chiefly in the treatment of the vomiting of pregnancy,[1-4] there remains no immediate way of measuring a relative deficiency of the vitamin and no direct chemical test for B_6 is available. The evidence for the therapeutic application of pyridoxine has, of necessity, been indirect and empirical, and open to dispute.[5-6]

Indirect measurements of deficiencies of this vitamin can be made, however, by observing its effect on the metabolism of tryptophan.[7-8] When tryptophan, one of the essential amino acids, is taken orally by a B_6-deficient animal, the abnormal metabolite, xanthurenic acid, is excreted in the urine. This also occurs in the human subject,[9] and is immediately corrected by the administration of pyridoxine. Employing this test, Sprince and co-workers[10] and Wachstein and Gudaitis[8, 11] report evidences of a relative deficiency of vitamin B_6 in pregnancy.

The present brief report is concerned with this test as an index of the pyridoxine status of the normal pregnant patient. Ten grams of tryptophan* was administered orally at night, and beginning two hours later a 10 hour specimen of urine collected. From the time of taking the tryptophan to the conclusion of the test, no other food or fluids were consumed. The xanthurenic acid excreted was determined colorimetrically, using the technique of Rosen, Lowy, and Sprince,[12] as modified by Wachstein and Gudaitis,[8] and expressing the result in milligrams of xanthurenic acid excreted per total 10 hour period. Using this technique, recovery experiments of measured amounts of pure xanthurenic acid† added to urine showed statistically reliable results with an average recovery of 107.2 per cent.

A total of 48 patients were studied, the individual tests being grouped to provide controls both between the pregnant and the nonpregnant, and between the pregnant patients who received pyridoxine and those who received placebos or other B fractions.

Results

A. XA Excretion After Tryptophan in Normal Men and Women.—

In 12 normal subjects, 9 women and 3 men, between the ages of 23 and 45 years of age, the excretion of XA after tryptophan administration varied

*Obtained from Merck & Co., Inc., Rahway, New Jersey, through the courtesy of Dr. R. A. Peterman.

†Obtained from Sharpe & Dohme, Inc., West Point, Pa., and from the Ortho Research Foundation, Raritan, N. J., through the courtesy of Dr. L. E. Arnow and Dr. Fred Rosen, respectively.

from 4 to 41 mg. per 100 hours of excretion. The average excretion was 17 mg. These results are almost identical with those obtained by Wachstein and Gudaitis[8, 11] in their 24 hour tests.

B. Excretion of XA After Tryptophan in Normal Pregnant Women in Various Stages of Gestation.—

The test was performed on 14 women who were less than 48 hours post partum or were at various gestational periods. None of these women had any evidence of toxemia or any other recognized organic abnormalities. About half of the women in this group were living in a home for unmarried pregnant women. With one exception, the XA excretion values in this group ranged from 116 to 741 mg. per 10 hour overnight urine sample. The over-all average was 251 mg. The single value below this range (26 mg.) occurred in a woman at 25 weeks of gestation who was the only patient in the group who was receiving a vitamin supplement. This was in the form of a multivitamin capsule and contained 0.2 mg. of pyridoxine, taken one each day.

C. The Excretion of XA in Normal Pregnant Women in Various Stages of Pregnancy Who Received Pyridoxine Prior to Tryptophan.—

This group was comprised of 8 individuals, 4 of whom had delivered less than 48 hours prior to beginning the test. Four of them had had a previous XA determination. Each one was given 50 mg. of pyridoxine orally. In half of the group the pyridoxine was given 7 hours, and in the other half 10 hours, before the administration of tryptophan. All patients showed a reduction in the values of XA equivalent to those obtained in normal nonpregnant women and normal men. The over-all average of this group was 13 mg. This reduction in XA excretion was even more rapid than in the experiments of Wachstein and Gudaitis,[11] who gave a greater amount of pyridoxine over a longer period of time to their subjects. Although the series is small, these results together with those of Wachstein and Gudaitis demonstrate quite clearly the depressing effect on XA excretion of small amounts of pyridoxine. Apparently neither the stage of pregnancy nor the previous level of XA excretion influences the effect of the pyridoxine.

D. The Excretion of XA in Normal Pregnant Women Who Received Aspirin Prior to Tryptophan.—

This group was composed of 9 individuals, and served as a control for the group who received pyridoxine. Three of these women had had XA determinations 3 weeks earlier. All 9 of them received 4,800 mg. of aspirin over a 36 hour period prior to being given tryptophan. This series showed more variation than was expected. Two of the patients who had both tests showed an appreciable rise in XA excretion over a 3 week interval. The third patient showed a 32 per cent decrease in XA excretion following aspirin administration, although the value obtained (236 mg.) was still in the range found to be characteristic of pregnancy. Wachstein and Gudaitis[11] have noticed that pregnant women without abnormality may show appreciable differences in XA excretion when tested at various times in pregnancy. Of the 6 who had had no pre-aspirin testing, the XA determinations in 3 showed values consistent with those of normal pregnancy (164, 273, and 590 mg.). The remaining 3 patients showed XA values of 48, 60, and 64 mg. These are considerably lower than our previous results in pregnant women would indicate that they should have been, but were still higher than those obtained in normal nonpregnant women and normal men. If these results are representative, it can be concluded that aspirin will not depress XA excretion as much or as consistently as pyridoxine. The over-all average for this group was 233 mg., with a range of 48 to 590 mg. (Table I).

TABLE I. THE XA EXCRETION IN NORMAL PREGNANT WOMEN WHO RECEIVED ASPIRIN PRIOR TO TRYPTOPHAN

NAME	AGE	WEEKS PREGNANT	EXCRETION AFTER TRYPTOPHAN		EXCRETION AFTER RECEIVING ASPIRIN BEFORE TRYPTOPHAN	
			URINE VOLUME IN 10 HOURS (ML.)	XA* IN 10 HOURS (MG.)	URINE VOLUME IN 10 HOURS (ML.)	XA* IN 10 HOURS (MG.)
E. U. R.	20	39	227	347	420	236†
E. L. R.	15	39	824	132	950	250†
J. T.	17	40	230	239	400	411†
M. S.	20	28			325	60
A. J.	19	32			795	48
J. U. T.	17	40			567	164
D. S.	18	40			485	273
R. T.	23	38			642	590
C. G.	20	38			120	64

*The determination of XA includes the interfering substances.
†These three samples were done 3 weeks after the original test.

E. The Excretion of XA in Normal Pregnant Women in Various Stages of Pregnancy Who Received Nicotinic Acid Prior to Tryptophan.—

In an attempt to determine whether or not pyridoxine is the specific vitamin which will depress XA excretion, five patients received 200 mg. of nicotinic acid in the 24 hour period prior to taking tryptophan. The average XA excretion of this group was 221 mg., with a range from 78.3 to 452.3 mg. Nicotinic acid, in other words, does not share with pyridoxine the ability to lower the xanthurenic acid excretion as dramatically.

F. The Excretion of XA in the Newborn.—

The possibility that the pregnant woman does not have a deficiency of pyridoxine, but that the placenta "traps" it in the fetal side as it traps vitamin C[15-16] cannot be excluded. Accordingly, an attempt was made to determine the xanthurenic acid level in the urine of newborn children, both with and without the feeding of tryptophan. Such a study would be of value only to the extent that the finding of a neonatal deficiency would rule out the possibility of a one-way transfer across the placenta favoring the fetus and lowering the maternal reserves of pyridoxine. The tryptophan was put into solution with the addition of a small amount of sodium hydroxide, and 1 Gm. was fed by stomach tube. The urine was collected over the next 12 hours for XA determination. The difficulties in obtaining complete specimens of urine render the studies less than quantitative, but of the 5 babies (out of 17 studied) with complete retention of the feedings and accurate urine collections, the xanthurenic acid excretion ranged between zero and 97 mg. per 24 hours. In none of these cases could a deficiency be demonstrated in the baby which would correspond to the deficiency seen in the pregnant woman. None of the mothers was receiving a pyridoxine supplement.

Comment

It is quite evident from the foregoing that marked increases in XA can be detected, after tryptophan intake, in the urine of normal pregnant women as early as the second trimester of pregnancy. Others[10] have shown even more marked elevations in the XA values of pre-eclamptic, eclamptic, and certain pregnant patients with concurrent diseases. Sprince and associates[10] noted high values in several "normal" pregnant women who later went on to develop signs of eclamptogenic toxemia. The follow-up on our patients with

the higher values has not revealed any signs of toxemia of pregnancy to date. Wachstein and Gudaitis[11] stated that 10 of their 24 pregnant women studied one to two days after delivery had shown signs of toxemia at one time or another. The average XA value in this toxemic group was 314 mg. per 24 hours, while it was 191 mg. in the nontoxemic group. Our group of normal pregnant women in the last trimester of pregnancy had values of 280 mg. of XA per 10 hours. In view of the wide range in XA excretion in both groups studied by Wachstein and Gudaitis, and in our own series, plus the relatively small number of patients so far studied, it is impossible at this time to conclude that XA excretion reflects or indicates the presence of toxemia. Furthermore, the complete specificity of the reaction for deficiencies or relative deficiencies of vitamin B_6, while highly probable, is not provable from these data alone.

Little is known about the actual requirements of this vitamin by the human body. Even less is known of the requirement during pregnancy. Vilter and his co-workers[13] did not feel that the B_6 status was an important factor in the maintenance of normal pregnancy. From a study of diets, Hobson[14] found evidences of a lack of both nicotinic acid and pyridoxine. Since clinical manifestations of vitamin B_6 deficiency can be produced only under the most extreme experimental conditions, it seems unlikely that pregnancy itself would lead to such a deficiency in its early weeks. The newborn baby does not seem to share this maternal "deficiency" and the possibility that the placenta "traps" vitamin B_6 as it traps vitamin C on the fetal side cannot be excluded.

Summary and Conclusions

The administration of tryptophan leads to the excretion of xanthurenic acid in urine in the presence of a deficiency of vitamin B_6.

This procedure has been applied to pregnant and nonpregnant patients; to subjects receiving supplements of pyridoxine and subjects receiving placebos.

The results indicate a relative deficiency of B_6 in pregnancy, particularly demonstrable in the last trimester and the immediate postpartum period.

No deficiency could be demonstrated in the normal newborn infant, although the data are not conclusive.

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THE CRYSTALLIZATION PHENOMENON OF THE CERVICAL MUCUS IN THE DIAGNOSIS OF EARLY PREGNANCY

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THE first scientific study of the endocervical mucus was made in France. In 1837 the Frenchman, Donné,[5] reported that the secretion from a surface of squamous stratified epithelium is acid, while secretion from a surface of columnar epithelium is alkaline. It follows that vaginal secretions in reproductive life are acid, while endocervical mucus is of alkaline reaction. From England, 18 years later, originated the first report on cyclical changes of the cervical mucus. W. Tyler Smith[13] specifically stated that this mucus was thin and viscid in the week following the menstrual period. He concluded that the high viscosity of the mucus during the intermenstruum was "adapted for the preservation and ascent of the spermatozoa to the cavity of the fundus uteri."

The crystallization of the cervical mucus, first observed in 1945 by Papanicolaou,[7, 8] was described by him as "arborization." His findings were confirmed by Rydberg[12] who, in 1948, characterized the phenomenon as fern-leaf structure. Campos da Paz[2] of Brazil has explored this phenomenon thoroughly since 1951 and found it valuable for the study of the cyclic changes in the female sex organs.

This discovery offers interesting possibilities for the study of sterility and hormonal disturbances in women. Campos da Paz stated that in anovulation the crystallization phenomenon persists throughout the cycle; some time later, Roland[10] reported the same findings. Consequently, Campos da Paz[3, 4] as well as Roland recommended use of the crystallization (or fern) phenomenon as a pregnancy test in early gestation. According to both authors the crystallization phenomenon is absent or atypical in pregnancy.

Da Paz performs the test as follows:

> The ectocervix is initially cleaned with cotton or gauze. The mucus is then aspirated from the cervical canal, spread on a glass slide, dried by heat, and examined under the microscope with the magnification of 100 to 150 times.

Roland uses the same technique, except that he removes the cervical mucus by means of a wooden applicator stick.

Such an obviously simple test can be done in any doctor's office. It can be interpreted within a few minutes. According to Roland, it can be done as early as two days after the date of the missed period. All these facts would make the new test appear superior to the Aschheim-Zondek test and its modifications.

The authors of the new test themselves have pointed out certain limitations. They declared it unsuitable for women in the menarche or approaching the

menopause, as well as for women with irregular cycles or with endocrine disturbances. In addition, we have found that the test is of only limited value for still another group. Right after pregnancy, terminated by either full-term delivery, or by rupture of an ectopic pregnancy, or by abortion, women are amenorrheic for several weeks. Whether, during this period, there is a new pregnancy or not may present a diagnostic problem. The Aschheim-Zondek test, or one of its modifications, can generally be relied upon to determine the presence or absence of pregnancy, whereas the fern test, in such a case, is usable only if the crystallization phenomenon is present. Absence of the phenomenon, obviously, can indicate either that ovulation has not yet set in again, or that a new pregnancy is present.

Thus, a rather large percentage of women are ineligible for the test. Yet, if the authors' claim of 90 to 99 per cent accuracy could be substantiated, the test would be of great value, even in the restricted area of its applicability.

The present study was undertaken to check the practical value of the fern test for the diagnosis of early pregnancy. We[6] reported our first findings during the discussion of Campos da Paz' lecture at the First World Congress on Fertility and Sterility, in May, 1953, in New York. At this time we already expressed doubts concerning the accuracy of the test as a means of diagnosing early pregnancy. Meanwhile, we have learned from Studdiford[14] that several members of his staff at Bellevue Hospital, New York, among them Kuppermann and Kleegmann, are entertaining similar doubts. Our own study, continued after the Congress and now concluded, has confirmed our earlier negative views.

In order to ensure follow-up and complete supervision, this study was limited to private patients only. The technique used was the same as Campos da Paz', except that we took two smears every time instead of one, in order to enable both of us to examine each specimen independently. On comparison our findings turned out identical, without exception. No patients under 20 years of age and no menopausal or suspected menopausal patients were selected. Women still amenorrheic after a recent pregnancy were also excluded. Our material includes only women with a history of regular menstrual periods, overdue for at least two days, according to their longest recorded interval. The presence or absence of pregnancy was established in every case either by an Aschheim-Zondek test (or one of its modifications), or by subsequent clinical observation. Only cases in which pregnancy or nonpregnancy had been established beyond doubt were used. This high selectivity accounts for the reduced number of cases presented in this study: of the many women tested by us, only 71 were considered eligible for evaluation.

TABLE I. RESULTS OF THE FERN TEST IN 71 CASES

Correct		
a. Correct positive: no fern, pregnant	33	
b. Correct negative: fern present, not pregnant	6	
Probably correct		
No fern, A.-Z. doubtful (endometrial biopsy while bleeding: decidua)	1	
		40
Wrong		
a. Wrong negative: no fern, not pregnant	31	
b. Wrong positive: fern present, pregnant	0	
		31
Fern test correct	57 per cent	
Fern test incorrect	43 per cent	

Two of our cases of proved pregnancy showed atypical fern. In contrast to the originators of the test, we could not find that women with atypical fern will subsequently abort. On the other hand we had one woman who showed no fern pattern, but who subsequently had an early abortion, as was proved by endometrial biopsy.

In all instances of definitely established pregnancy the test was correct, i.e., positive. It was, however, incorrect in 84 per cent of the cases where delay of menstruation was *not* due to pregnancy; in other words, in the case of 31 out of 37 women it indicated pregnancy where there was no pregnancy. In order to be of value for the diagnosis of pregnancy, a test must be reliable in the positive as well as in the negative. Aschheim,[1] for instance, reported, in 1933, on 2,000 women who had been tested with his method. He had 98 per cent correct positives, and 99.5 per cent correct negatives, or an over-all 98.9 per cent correct results.

It is Roland's contention that failure of the test can be due only to misinterpretation of atypical as typical fern. This does not account for the fact that smears of 31 nonpregnant women (examined, as was our practice, independently by both of us) showed no fern pattern at all, whereas the presence of fern would have been in accordance with the clinical picture of nonpregnancy. It may be of interest that, of this group of 31, 9 women were definite psychoneurotics (7 undergoing psychotherapeutic treatment); 5 had developed pregnancy anxiety prior to the delay of period; one patient was under severe emotional strain, caused by a suspicious cervical lesion; one had just lost her husband; and 3 women, including 2 sterility cases, had a strong desire to become pregnant.

Comment

As already observed by Papanicolaou, the arborization phenomenon of the cervical mucus undergoes certain changes during the normal menstrual cycle. It becomes typical at the approximate time of ovulation, and it decreases and finally disappears in the subsequent days of the cycle. Papanicolaou further stated that the crystallization phenomenon is absent during pregnancy. These findings have been corroborated by Campos da Paz and Roland. Our study confirms their findings only as far as cases of definitely proved pregnancy are concerned. However, there is no basis for the assumption that because the crystallization phenomenon is absent in pregnancy, it must be present in all instances of menstrual delay not due to gestation. The cervical mucus of women whose delay is caused by hyperestrinism and anovulation will show the arborization pattern, but only a small percentage of postponed menses is due to this condition.

Neither Roland nor Campos da Paz supplies statistics relating to the absence of the crystallization phenomenon in cases of menstrual delay not due to pregnancy. Most of our patients in this category had no fern pattern, a fact that seems to support the generally accepted opinion that a variety of factors—psychological, environmental, and others—may delay the onset of the period, without preventing ovulation. Thus, a trauma in the preovulatory part of the cycle may postpone ovulation and, consequently, delay menstruation. Evidently, the same trauma appearing in the second half of the cycle will not influence ovulation while causing postponed menstruation.

Two nonpregnancy cases from our series seem suggestive of this mechanism. The cervical mucus of both women, examined in a late stage of premenstruation (of a delayed period), revealed only cellular elements, identical with those found during the week preceding a regular period on time.

CASE 1.—Mrs. P. M., aged 37, whose menses began at the age of 12, occurred every 28 days, and lasted 3 days, was a gravida ii, para ii. She had lost her husband eighteen months before. For the last six months she had been dating another man. First sexual relations occurred five days before the period due on May 2, 1953. On May 9 there was no crystallization phenomenon. The patient was very agitated, partly due to guilt feelings and partly because her diaphragm had not been checked since her husband's death. Everything possible was done to reassure this patient; in addition 1 c.c. of Prostigmin 1:2,000 was injected. Menses commenced on May 14 and have remained regular since.

CASE 2.—Mrs. G. T., aged 37, whose menses had started at the age of 12, occurring every 28 days, and lasting 4 days, was a gravida vi, para iv, who had had two regular periods since her last delivery. The last menstruation was on Aug. 31, 1953. On September 23, five days before her expected period, the question of birth control was discussed, and the patient suddenly realized that her type of contraception was inadequate. She was seen again, in a state of anxiety and distress, on September 30, two days after her period had been due. At this time, no crystallization was noted in the cervical mucus. The patient was reassured and 1 c.c. of Prostigmin 1:2,000 was injected. Menses commenced two days later.

In the few cases of delayed menses where the crystallization phenomenon was present—17 per cent—the delay may have been due to hyperestrinism or anovulation. But since we have no endometrial biopsies we cannot prove or disprove such a theory.

According to Mme. Roussel,[11] the fern phenomenon is absent throughout the cycle in cases of severe cervicitis. We may, therefore, assume that severe cervicitis is still another condition precluding the crystallization phenomenon from use as a pregnancy test. Some of our own wrong positive results (cases of amenorrhea, no pregnancy, and no fern formation) may have to be attributed to this condition. Pye[9, a and b] originally also felt that the fern phenomenon could be used as a quick diagnostic method in early pregnancy, whereas Roussel found that its only value was for the differential diagnosis of amenorrhea. More recently, Pye[9, c] has concurred with her opinion.

Summary and Conclusion

1. The purpose of the present investigation was to examine the reliability of the crystallization phenomenon as a test for early pregnancy.

2. We have used exactly the same technique as Campos da Paz and Roland.

3. The cervical mucus of 71 women with delayed periods was examined.

4. The over-all accuracy of the test was 57 per cent; it was 100 per cent correct in all instances of proved pregnancy; in the cases of menstrual delay not caused by pregnancy, however, the test was incorrect in 84 per cent.

This investigation indicates that the test based on the crystallization phenomenon of the cervical mucus, in its present form, is of only very limited value for the diagnosis of early pregnancy.

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RAPID DETERMINATION OF PLASMA FIBRINOGEN*

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SEVERE grades of abruptio placentae and some instances of intrauterine death of the fetus are sometimes accompanied by a fibrinogenopenia sufficient to account for noncoagulability of the blood. It is our belief that the cause of this phenomenon is the direct release of thromboplastic proteins from the gravid uterus into the maternal circulation.[1] The critical level of plasma fibrinogen at which uncontrollable hemorrhage may occur is approximately 100 mg. per cent. The fact that deaths may be averted by the prompt use of fresh blood (in contradistinction to bank blood) or human fibrinogen (e.g., Parenogen, Cutter) makes it imperative to recognize the deficiency promptly.

Most laboratory procedures for determining plasma fibrinogen require too much time for clinical safety. Gravimetric methods, for example, require drying the fibrin to constant weight in the oven for many hours. Salting out procedures followed by Kjeldahl nitrogen determinations may require half a day. Methods based upon the determination of biuret or tyrosine in a fibrin clot can be accelerated by adding an excess of thrombin to the clotting mixture. The time required to digest the clot and to develop and measure the color is added to the time required for the present method. Losner and associates[2] published a rapid turbidometric method, but in our hands it has not been suitable for the determination of low fibrinogen levels. The whole blood dilution assay suggested by Schneider[3] is too rough an approximation to be dependable.

Principle

The method herein described requires a centrifuge and a balance sensitive to at least 2 mg. Results, with a standard error of 17 mg. per cent, can be reported within 30 to 45 minutes. Oxalated plasma is diluted with saline, then calcium chloride and thrombin are added in quantities sufficient to convert 100 per cent of the fibrinogen to fibrin in 10 minutes at 37° C. The fibrin is collected, blotted dry, and rapidly weighed. The fibrinogen concentration is determined from an equation relating it to the moist weight of the clot.

The equation was derived from a line of regression fitted to 36 points by the method of least squares. The points were determined by appropriate dilutions of plasma samples from several individuals in order to reproduce a range of fibrinogen concentrations from 13 to 474 mg. per cent. The actual concentration of fibrinogen in each sample was determined by the method of Greenberg and Mirolubova.[4] The standard error of the estimation from moist clot weight was

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found to be ± 17 mg. per cent. This was found from the expression: $S_y = \sqrt{\frac{d^2}{N}}$ where d is equal to the difference between the actual value of y (fibrinogen concentration) and the theoretical value obtained by substituting experimental values for x (moist weight of clot) in the equation for the regression line. The latter is represented by: $y = 4.3x + 14.6$.

Method

Reagents.—

0.9 per cent sodium chloride solution.

1.0 per cent calcium chloride solution.

Thrombin (Parke-Davis Topical). Each 100 mg. contained in the vial is dissolved in 25 ml. 0.9 per cent sodium chloride and 25 ml. of glycerol. This solution keeps for many months in the freezing compartment of the refrigerator.

Procedure.—Ten milliliters of oxalated blood is centrifuged to remove red cells. During this time, 150 ml. of saline in a beaker is brought to 37° C. Five milliliters of plasma is mixed with the saline and 12.5 ml. of 1 per cent calcium chloride solution and 2.5 ml. of thrombin solution are added and promptly stirred thoroughly but briefly with a glass rod. The glass rod is left in the mixture. After incubation at 37° C. for about 8 minutes the clot is gathered on the rod by alternate gentle rotation and pressure against the sides of the vessel. The collection usually requires about 2 minutes so that the total incubation time is 10 minutes. When most of the fluid has been pressed out against the sides of the vessel the clot is slipped down the rod to a double layer of Whatman's No. 50 filter paper by means of gentle pressure with forceps. A second double layer of filter paper is pressed down on the clot. The clot is moved to a dry spot on the paper and again pressed with dry paper. This procedure is repeated until no visible moisture is left on the paper. The clot is then weighed rapidly, again pressed between filter paper and reweighed. This is repeated until two weights check within 5 per cent. (Under the usual humidity conditions of San Francisco, this requires 3 to 4 weighings; but in hot, dry climates the rapidity of achieving constancy would have to be evaluated.) The concentration of plasma fibrinogen (y) is then calculated from the weight of the clot (x) and the equation $y = 4.3x + 14.6$.

Summary

A procedure for determination of plasma fibrinogen, accurate within a standard error of 17 mg. per cent, has been developed especially for cases of severe abruptio placentae. Results can be reported within 30 to 45 minutes from the time a request is made. The method is based on a determination of the moist weight of a fibrin clot and the use of an equation for converting this weight to plasma concentration.

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Department of Case Reports New Instruments, Etc.

AMNIOTIC FLUID EMBOLISM

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IN 1941, Steiner and Lushbaugh[1] described for the first time the entity of amniotic fluid embolism. Previous to this, sudden death in labor or in the immediate puerperium was ascribed to obstetric shock, postpartum hemorrhage, or acute pulmonary edema of pregnancy, in cases where no other definite pathology could be demonstrated as the cause. Since the original communication in 1941, a total of 57 cases has been reported. The incidence usually has been reported as about one in 8,000 deliveries, although one survey shows no cases of this type in ten years' experience in a teaching hospital.

Amniotic fluid embolism usually develops in older multiparas with otherwise normal histories of past health and obstetrical experience. Their symptoms develop during labor or shortly following delivery. The labor is characteristically violent in nature, the membranes have ruptured, and meconium is present in the amniotic fluid. The individuals are frequently past term, and in a considerable number of cases the fetus has been dead for some time. It has been suggested that the character of the pains may be so violent because of the frequent association of some degree of placental separation.

The chief symptoms of amniotic fluid embolism are those of restlessness, nausea, vomiting, chills, shortness of breath, and rapid or absent pulse. At the same time, the blood pressure is at shock levels or cannot be obtained. Cyanosis develops quickly, and coma and death occur immediately or within a few hours. The whole picture is similar to that of anaphylaxis and has often been described as an anaphylactoid type of reaction. The shock present in this kind of embolism often cannot be attributed to the amount of initial blood loss, as it is frequently manifested before the bleeding tendency has developed. It is more comparable to cardiovascular collapse. Pulmonary edema occasionally develops, and corresponding lung findings and frothy sputum may be present, with entirely normal heart findings. If a patient survives the initial shock reaction, an uncontrollable bleeding tendency soon develops from the uterus, gums, and at the sites of venipuncture or incision. Blood drawn for testing fails to clot, and at postmortem examination there is no evidence of clot formation in the large vessels or the heart.

When amniotic fluid enters the maternal circulation, it has a marked thromboplastic action. It produces rapid clot formation, followed by a further defibrination of the blood, which results in the excessive bleeding tendency. This faulty clot formation can be demonstrated in blood samples drawn. In addition, the blood serum exerts a lytic action, so that formed clots tend to disintegrate. If the blood samples taken from patients with amniotic fluid embolism are centrifuged or allowed to stand, they eventually show a lighter layer above the leukocytic layer. This layer contains amniotic fluid elements of squamous cells, mucus, meconium derivatives, and vernix caseosa. It has been suggested that, in suspected cases of amniotic fluid embolism where postmortem examination is refused, blood withdrawn from the right side of the heart would show this layering characteristic. A diagnosis can be established from study of the superficial layer in smear or block.

Possibly there have been a number of unrecognized sublethal cases of amniotic fluid embolism. One case cited, which was recognized, occurred in Boston. Sudden shock developed, followed by diffuse lung pathology as found by physical examination and x-ray. Shortly thereafter, hemorrhagic tendencies became manifest and were successfully controlled by multiple transfusions of whole blood and administration of fibrinogen. Although the bleeding was controlled, there was complete suppression of kidney function following the multiple transfusions. After the patient was transferred to Peter Bent Brigham Hospital, an artificial kidney was employed. Kidney function ultimately returned, and the patient was finally discharged. It remains to be seen whether or not she will develop Sheehan's syndrome at a later date.

Case Report

The case here reported is the first one diagnosed as amniotic fluid embolism in the history of Mercy Hospital. This is an incidence of one in over 40,000 deliveries.

The patient was a 39-year-old woman, gravida iii, para ii. The estimated date of confinement was Feb. 1, 1954. On January 27, she was admitted to the hospital at 2:15 P.M. Throughout the afternoon, she had irregular pains of poor quality. At 7 P.M., a sterile vaginal examination showed the cervix to be dilated to approximately 3 cm., with membranes bulging. The membranes were ruptured to promote more rapid progress. The fluid that escaped was not meconium stained at that time.

At 7:40 P.M., the patient vomited. At 7:55 P.M., a convulsion was reported, followed by labored respiration, cyanosis, and unobtainable blood pressure. Oxygen was administered under pressure, and artificial respiration was used with an airway at the same time. Intravenous glucose was started, caffeine sodium benzoate was administered into the intravenous tubing, and, when no heart sounds could be heard, Adrenalin was injected into the heart.

At 8:09 P.M., the patient was pronounced dead, but fetal heart sounds could still be heard. A rapid postmortem cesarean section was performed, with delivery of a living female infant in poor condition. The infant responded to stimulation and oxygen, and, thanks to the use of the Airlock, the infant survived and is at present progressing satisfactorily. It will not be evident for some time whether the anoxia has had a deleterious effect on the brain.

The autopsy done the following day disclosed no significant gross abnormality. The brain showed no abnormality or evidence of hemorrhage. The heart presented a normal myocardium, normal valves and vessels. Grossly, the lungs showed slight congestion of the lower lobes. The pulmonary vessels were grossly normal. The liver was normal, but the kidneys showed slight congestion.

The significant pathology was shown in microscopic study of the lung sections. Here, the small arterioles were plugged with epithelial cells and amorphous material derived from the amniotic fluid. The same type of material plugged the capillaries of the alveolar walls. There was no significant abnormality in the other tissues studied. These microscopic findings are diagnostic for amniotic fluid embolism.

Summary

The occurrence of amniotic fluid embolism is most frequent among older multiparas with normal courses of pregnancy and normal past histories. In many cases, the delivery is of a known dead fetus, and often the fetus is lost because of coincidental disease. Frequently the fetus is quite large and postmature, and these factors lead to obstetrical difficulty. All of these conditions contribute to the presence of meconium in the amniotic fluid.

When amniotic fluid embolism occurs, its onset is usually so rapid and so violent, with symptoms of such profound degree, that therapeutic measures are of no avail.

In the case reported here, the infant survived because of excellent cooperation and equipment immediately available. In one other instance of a living infant obtained by postmortem cesarean section following amniotic embolism, the infant is reported to have lived only twelve hours.

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A FATAL CASE OF AMNIOTIC FLUID EMBOLISM*

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THIS case is of special interest because the point of entry of the amniotic fluid was located.

The patient, a gravida v, para iii, had an uneventful pregnancy. On April 18, 1950, she was admitted to Fairview Hospital about four hours after the onset of labor with the cervix dilated 2 cm. Labor progressed slowly. She was given Demerol, 75 mg., and scopolamine, 1/200 grain. The pains became more regular and the cervix dilated to 3 cm. She was taken to the delivery room 45 minutes later because of marked nausea with the pains. She twice vomited small amounts of greenish liquid. She was drowsy and rested well between pains. One-half hour later she had an involumtary defecation and urination and 45 minutes later the nurse made the following entries: "The patient turned on side by herself, became rigid with head thrown sharply back. Very cyanotic and does not respond, respirations gasping. Pulse imperceptible. B.P. 130/60. Patient dead."

An autopsy was performed by Dr. Koucky on the same day. The lungs were moderately heavy and edematous. The left lung weighed 450 grams and the right weighed 440 grams. The lower lobes were partially atelectatic. The bronchi and the trachea showed no foreign material, and the pulmonary arteries showed no emboli. No air was present in the heart.

Examination of the external surface of the uterus showed no suggestion of trauma, hemorrhage, or other changes. The uterus contained a normal term female infant, in left vertex anterior presentation. The membranes were ruptured with about 200 c.c. of thick greenish fluid in the uterine cavity, and this was present in the interspaces between the legs and the arms and in the space around the neck. The fetal head was in the lower uterine segment. The wall and the muscle of the lower uterine segment were bare for distances varying from 2 to 4 inches. On the exposed posterior wall of the uterus, a small depression was observed which, when explored with the tip of a forceps, proved to be a sizable channel (Fig 1). A rubber catheter of the type used in male catheterization easily passed through the opening into the interior of the uterine wall and appeared in the large veins of the right broad ligament. Blood recovered from the right common iliac vein and from the lower vena cava, when spread out on the white porcelain tabletop, showed numerous flakes of green mucoid material. One of the larger pieces was about 1 mm. in diameter and 5 or 6 mm. in length.

Approximation of the fetus into its original position within the uterus indicated that the opening into the uterine vein was in about the same position of the space formed by the fetal neck and the small parts.

Microscopic study showed about the same picture in all lobes of the lungs. In every section there were many small arterioles and capillaries containing foreign material made up of squamous epithelial debris, amorphous material, mucus, and leukocytes (Fig. 2). A few foci of leukocytes were present in the lung parenchyma which had the appearance of beginning exudation.

Two impressions were received from the microscopic study of the lungs in this case. The early exudative reaction suggested that the embolism of amniotic sediment was not a terminal explosive event but had been going on for many minutes or even hours. Perhaps the patient's nausea, vomiting, involuntary bowel movement and urination indicated the be-

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ginning of the embolism. The second impression was that the degree of embolism produced only moderate vascular occlusion and that death was due to causes other than mechanical obstruction. It is very likely that "shock" similar to that caused by foreign material in a blood transfusion may have been the final cause of death.

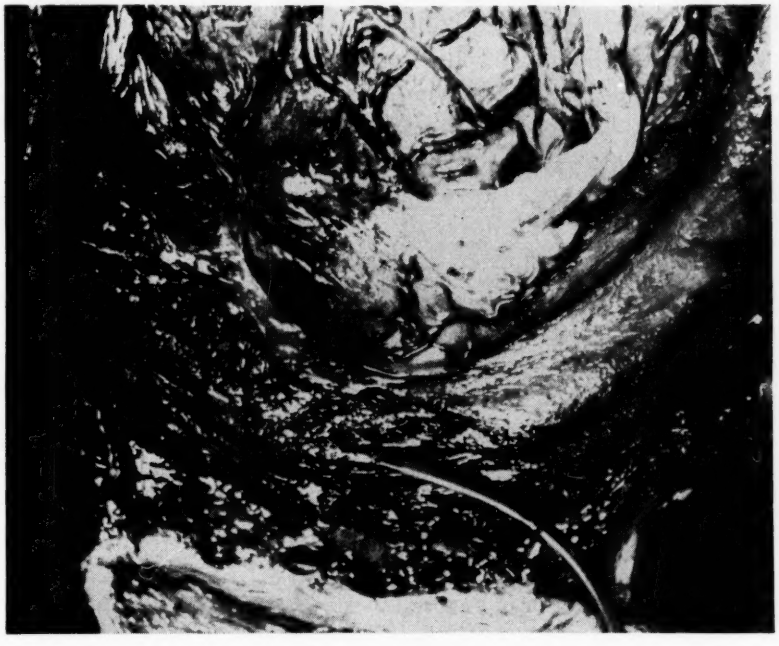

Fig. 1.—Posterior wall of uterus with male catheter in small depression communicating with interior of uterus and large veins of right broad ligament.

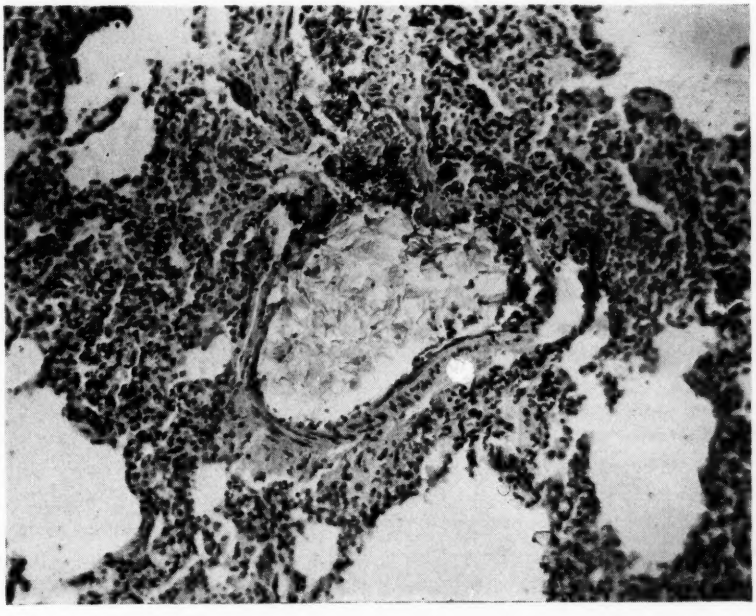

Fig. 2.—Small arteriole in lung filled with particulate matter.

Study of reported cases indicates that there is no specific etiology. It is obvious that congenital disturbances in structure or position of blood vessels cannot be a factor, because the majority of patients have had previous pregnancies without complications. Steiner and Lashbaugh suggest that intact membranes or closure of the uterine outlet by the fetal head, together with hard uterine contractions, may force amniotic fluid into the placental veins. Leary and Hertig demonstrated squamous cells from amniotic fluid within the placenta and its membranes, and suggested that such extravasations are not uncommon in labor. Landing found squamous cells present in the uterine vessels in from one-third to one-fourth of the uteri removed as operative or autopsy specimens in cases of placenta accreta, ruptured uterus, cesarean section, retention of placenta, and premature separation of the placenta. In three of his cases, squamous cells from the amniotic fluid were also found in the lungs. These studies indicate that the entry of amniotic fluid into uterine vessels may not be uncommon and that subclinical or mild forms of amniotic fluid embolism might occur.

In about one-half of the reported cases, some tear or surgical incision into the uterus, cervix, or placenta was present. This case is unique in that a very large communication between the uterine cavity and the maternal circulation was demonstrated.

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HEMOLYTIC DISEASE OF THE NEWBORN DUE TO BOTH ANTI-Rh (D) AND ANTI-KELL (K) ANTIBODIES

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HEMOLYTIC disease of the newborn due to anti-Rh or anti-Kell antibody is well known. The finding of these two immunologically distinct antigen-antibody systems accounting for hemolytic disease has been only briefly mentioned.[2] We wish to describe in detail the fifth reported case with anti-D and anti-K antibodies. Opportunity is taken to describe such an occurrence with particular reference to the nature and strength of these antibodies.

D. L., a 20-year-old white woman, gravida ii, para i, was admitted, at term, to the Albert Einstein Medical Center, Southern Division, on May 25, 1953. Her pregnancy was normal save for a prolonged labor which necessitated a cesarean section. An anti-Rh (D) antibody of 1:64 in albumin and 1:1 in saline was found on admission. A female infant was born by cesarean section on May 26, 1953, and weighed 7 pounds, 12 ounces. There was slight pallor, moderate icterus, but no hepatosplenomegaly, adenopathy, purpura, or glossitis.

The examination of the cord blood showed: erythrocyte count 4.02 million hemoglobin 15.6 Gm. (100 per cent), leukocyte count 20,200 with 7 per cent band forms 23 per cent segmented forms, 64 per cent lymphocytes, 1 per cent monocytes, 4 per cent metamyelocytes, 1 per cent myelocytes; 13 nucleated red blood cells per 100 white blood cells were noted. The peripheral smear showed polychromatophilic macrocytes, target cells, and spherocytes. The serum bilirubin of cord blood was 1.5 mg. per cent.

O Rh-negative donor cells were not agglutinated when incubated in the mother's serum. These cells, however, were now found to be agglutinated by the Coombs reagent whereas a negative result was found prior to incubation, i.e., the immunologic incompatibility was detectable only by the indirect Coombs test and not by any other serologic method. Thus it was demonstrated that another immunologic incompatibility besides the Rh system caused hemolytic disease in the child. The immunologic procedures to define this reaction are presented in Table I.

Moreover, an indirect Coombs test performed on a panel of Rh-negative Kell-positive cells previously incubated in the mother's serum gave positive results whereas negative findings were obtained with Rh-negative Kell-negative cells. Thus an anti-Kell antibody was demonstrated in the maternal serum. Since the infant was Kell positive as well as Rh positive, the hemolytic anemia was due to isoimmunization by these two factors.

An exchange transfusion using O Rh-negative, Kell-negative blood was successfully completed and the infant discharged on June 4, 1953. The blood count continued to fall slowly so that a supportive transfusion of 100 c.c. of packed cells was required. The child has since been completely well.

TABLE I.

	BLOOD TYPES											
	A_1	B	C	D	D^u	E	c	e	M	N	P	K
1. Father	·	·	+	+		·	·	+	+	+	·	+
2. Mother	+	·	·	·	·	·	+	+	+	+	·	·
3. Child	+	·	+	+		·	·	+	+	+	·	+

			IMMUNOLOGIC TESTS*									
			1:1	1:2	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512
Mother's serum (saline)	+ DK cells	+ Coombs reagent	++++	++++	+++	++	+	+	+	±	·	·
Mother's serum (saline)	+ dK cells	+ Coombs reagent	++	+	+	+	+	±	·	·	·	·
Mother's serum (saline)	+ Dk cells	+ Coombs reagent	+	+	+	+	±	·	·	·	·	·
Mother's serum (saline)	+ dk cells	+ Coombs reagent	·	·	·	·	·	·	·	·	·	·
Mother's serum (albumin)	+ DK cells		+++	++	++	+	+	+	+	±	·	·
Mother's serum (albumin)	+ dk cells		±	±	·	·	·	·	·	·	·	·
Mother's serum (saline)	+ Dk cells		+	±	·	·	·	·	·	·	·	·
Mother's serum (saline)	+ dK cells		±	·	·	·	·	·	·	·	·	·
Mother's serum (saline)	+ Dk cells		+	·	·	·	·	·	·	·	·	·
Mother's serum (saline)	+ dk cells		·	·	·	·	·	·	·	·	·	·

Anti-C antibody not present in either saline or albumin dilution of mother's serum.

*+ positive.
± doubtful.
• negative.

Comment

The occurrence of two distinct immunologic systems accounting for hemolytic disease was observed by the routine incubation of O Rh-negative blood with the mother's serum and testing its compatibility with the Coombs reagent. Had this not been done, it would have been assumed that the hemolytic process was entirely due to an anti-Rh antibody. The finding of an anti-Kell antibody necessitated the administration of Rh-negative Kell-negative blood.

Approximately 10 per cent of Rh-negative bloods are Kell positive. Previous instances of hemolytic disease due to anti-Rh antibody could also have occurred with an anti-Kell antibody. These would not have been detected if the donor cells were Kell negative or if a Coombs test was not done on Kell-positive cells previously incubated in the mother's serum.

The anti-Rh antibody titer was much more active in albumin and saline than the anti-Kell antibody. Titrations employing the indirect Coombs showed them to be the same, the anti-Rh titer being 1:8, whereas the anti-Kell was 1:16.

Previous cases of isoimmunization due to anti-K have been associated with only slight-to-moderate degrees of anemia in the child. Their presence can be detected only by the use of the indirect Coombs technique. Since approximately 90 per cent of individuals are Kell positive, isoimmunization would be infrequent.

Summary

1. Hemolytic disease of the newborn due to both anti-Rh and anti-Kell antibodies is described.

2. The importance of an indirect Coombs test employing donor blood, mother's serum, and Coombs reagent before instituting exchange transfusions in hemolytic anemia of the newborn is emphasized.

We wish to thank Dr. Charles Mazer for permission to report the findings in this patient.

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METASTATIC CHORIONEPITHELIOMA CONCOMITANT WITH THE PRODUCT OF CONCEPTION

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NOTHING has been written about the presence of metastatic chorionepithelioma in conjunction with the product of conception still in utero. The reason perhaps is not because it does not occur but that it has escaped attention. It is known, however, that chorionepithelioma and the pregnancy from which it originated may coexist. Mathieu[1] is of the belief that when chorionepithelioma is found within two months after the passage or removal of hydatidiform mole the two conditions had coexisted.

Holman and Schirmer[2] in their fifteen-year survey of 426 cases of mole and 107 cases of chorionepithelioma on the Pacific Coast from 1936 to 1945, by using Mathieu's criterion, found that chorionepithelioma coexisted with hydatidiform mole in 42 per cent.

Applying Mathieu's criterion among our 43 cases of chorionic malignancy from 1950 to 1953, 27, or 62.79 per cent, coexisted with the product of conception. With the exception of 5 cases, the product of conception associated with the chorionic malignancy was hydatidiform mole.

One may not agree with Mathieu's criterion of two months but the following cases showed metastatic chorionepithelioma while the product of conception still existed in utero. In fact, the diagnosis of chorionepithelioma was made only from the manifestation of metastasis in 5 cases.

Briefly, the histories of the cases are as follows:

Case 1.—T. A., 30 years old, gravida viii, para vii, was admitted on Dec. 9, 1938, for the complaint of bleeding and labor pains at the eighth month of pregnancy. This was a case of twins in which one twin was a live, 8 months' fetus with its normal placenta and the other a hydatidiform mole. After the mole was expelled, the patient was delivered of a live fetus followed by its placenta. Soon after, she complained of headache, then became unconscious and died. Autopsy showed metastatic chorionepithelioma in the vagina, lungs, and brain.

Case 2.—(Private case of Dr. J. Villanueva.) During the fifth month of pregnancy the patient consulted her physician because of vaginal bleeding. The bleeding came from what appeared to be a cervical polyp which was removed and its bed cauterized. Biopsy of the tissue removed revealed chorionepithelioma. X-ray examination of the lungs showed shadows of metastasis. Less than three weeks thereafter, the patient died. There was no autopsy.

Case 3.—P. A., 38 years old, gravida ix, para viii, was seen in May, 1952. This was a case where the correct diagnosis was made only at autopsy. The patient was admitted in the medical ward for complaints of chest, abdominal, and sacral pains, cough and hemoptysis for one month before admission. There was no vaginal bleeding. She died after 7 days' stay in the hospital. The autopsy showed the uterus to be the size of a 4 months' pregnancy and filled with mole cysts. There were extensive hemorrhagic metastatic growths in the lungs, liver, brain, kidneys, and intestines, from which the patient died.

CASE 4.—I. A., 38 years old, gravida vii, para ii, was admitted to the hospital on Aug. 4, 1952, for hypogastric pain, dysuria, frequent desire to defecate, and slight bloody mucoid vaginal discharge. The date of her last menstruation could not be ascertained. In July she had chills, fever, and cough. She went then to San Lazaro Hospital where she was told that the x-ray of her chest showed "weakness of the left lung." The cough persisted and she had meat-washing-like expectoration. There was a strong history of tuberculosis in her family. Her father had died of tuberculosis. One sister had a chronic cough.

Physical examination showed that she was thin and undernourished, the lower abdomen was tender, and there was slight vaginal bleeding.

The diagnosis given by the admitting physician was ectopic pregnancy. This was later changed to uterine pregnancy with pelvic infection. The frog test of the urine was positive. She persistently complained of pain in the lower abdomen, pain in the chest, and cough. She went home on Aug. 10, 1952.

On Oct. 13, 1952, she went to the Emergency Section on Floor 7 because of persistent pain in the chest, cough, and abdominal pain. X-ray of the chest for tuberculosis was made and the report given was that of pulmonary metastasis. She was much emaciated. The lower abdomen was bulging, painful, and tender. The uterus was enlarged to the size of a 3 months' pregnancy, markedly tender and fixed. She was brought home in serious condition and died on October 14. There was no autopsy.

CASE 5.—L. B., 24 years old, gravida vi, para iv, was seen on Sept. 7, 1952. Her last menstruation was on July 5, 1952. In August she had four bouts of vaginal bleeding, hypogastric pain, and vomiting. The vomitus had blood streaks. When seen in September or two months after her last menstruation, the size of the uterus was that of a 3 months' pregnancy. Hydatidiform mole was suspected, but because there was no bleeding, and amniotic fluid seemed to be present, the diagnosis of hydatidiform mole was not made and she was sent home with the advice to return if bleeding should occur. On October 3 she returned to the hospital because of profuse vaginal bleeding. On examination, the bleeding was seen to come from a vaginal metastatic tumor. On the following day, the vaginal metastasis was surgically removed followed by total hysterectomy with the mole in situ and left salpingo-oophorectomy. On sagittal section, the uterus was seen to be filled with small mole cysts. In the center was some mucous fluid which had the characteristics of amniotic fluid.

On October 17, x-ray of the lungs showed shadows of metastasis so the lungs were treated by deep x-ray daily until November 20 when they became negative. The frog test on November 21 was also negative.

CASE 6.—P. D., 29 years of age, gravida iii, para ii, was admitted on March 13, 1953, for the complaint of dyspnea, pain in the chest, vaginal bleeding, and edema of the lower extremities. On admission, she was dyspneic with a temperature of 39° C., pulse 120, respiration 46, blood pressure 140/90 mm. Hg. She had been amenorrheic for 5 months but the uterus had the size of a 7 months' pregnancy. There were no fetal parts or fetal head. X-ray of the chest showed the heart slightly enlarged and metastatic shadows in both lungs. The diagnosis was that of malignant mole with pulmonary metastasis.

She was given digitalis and when she felt better, on the third hospital day, a hysterectomy was performed and the mole removed in situ. The left ovary appeared normal so it was not removed. The lungs were treated by deep x-ray from the third postoperative day until April 6 when the lungs became negative by x-ray. The frog test of the urine also became negative on this date.

Comment

Case 1 was a case of double-ovum twins in which one twin was normal and the other a malignant mole with metastatic chorionepithelioma in the vagina, lungs, and brain, from which the patient died. It was not possible to save the life of this patient.

Case 2 was diagnosed only by the biopsy of metastatic chorionepithelioma in the cervix and the presence of metastasis in the lung, from which the patient died. Since there was no autopsy, one could not tell if this was a case of twins where one twin was a mole giving rise to metastatic chorionepithelioma.

Case 3 was admitted to the hospital for symptoms of multiple metastases in different organs from which she died. With the early occurrence of the multiple metastases in different organs, it was not possible to save the life of the patient.

Case 4 was a misinterpreted case. The patient was thought to have tuberculosis with a normal uterine pregnancy and pelvic infection. The true condition of this patient was not known until the x-ray of the lungs revealed pulmonary metastasis. If she had been operated on when first admitted and the lungs treated by x-ray, she might have been saved.

Case 5 was cured, I believe, because at the first occurrence of bleeding from the vaginal metastasis the tumor was immediately removed and the uterus was also excised with the malignant mole in situ.

The same may be said of Case 6. On the discovery of the lung metastasis, as soon as the patient could stand the operation, the uterus was removed together with the malignant mole in situ and the lungs treated by x-ray afterward. The uterus was greatly distended. Had curettage been performed, it might have resulted in death from severe postpartum hemorrhage besides promoting further metastases.

Summary and Conclusions

Six cases of metastatic chorionepithelioma occurring in conjunction with the products of conception in utero are presented for the first time. In three of the cases the products of conception were known to be mole. One was known to be a case of twins, with one twin a normal 8 months' living fetus with its normal placenta, and the other twin a mole with metastatic chorionepithelioma.

Of the 6 patients, only 2, or 33.33 per cent, were saved. They were saved because of the early treatment of the metastatic growths and the early performance of complete hysterectomy with the mole in situ.

The presence of metastasis concurrent with pregnancy, which usually is a mole, calls imperatively for immediate treatment of the metastasis by x-ray if it is pulmonary or by surgery if the growth is in an accessible place like the vagina or vulva. At the same time the site of pregnancy, be it the tube or the uterus, should be extirpated in toto together with the abnormal product of conception in situ, to remove the focus of malignancy from which further metastases may arise.

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RETAINED PLACENTA INCARCERATED IN THE RUDIMENTARY HORN OF A DOUBLE UTERUS

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ABNORMALITIES in the embryonic fusion of the paramesonephric ducts may result in malformations which may seriously affect the management of obstetrical cases. There have been described almost a hundred cases of pregnancy in the rudimentary horns of double uteri which do not communicate with the main uterine cavity.[1] Bettman[2] described pregnancy in one horn of a double uterus with dystocia resulting from the blocking of the pelvic cavity by the nonpregnant horn.

Falls[3] has emphasized the increased incidence of complications accompanying pregnancy in a uterus arcuatus, a form of bicornuate uterus in which fusion is almost complete. This type of double uterus is associated with increased frequency of prematurity, postmaturity, prolonged first stage of labor, abnormal presentations, intrauterine fetal death, and retained placenta.

Schickele[4] has reported instances in which the pregnancy developed in a diverticulum from the uterine cavity, so that the fetus lay in a sac surrounded by uterine muscle, and connected with the main uterine cavity only by a narrow passage.

This case is that of a uterus bicornis unicollis with one rudimentary horn (the right), connected to the main endometrial cavity and the left horn through a small stenotic passage. The placenta was implanted in the small rudimentary horn with the umbilical cord passing through the os to the fetus lying in the larger left horn and lower uterus. To my knowledge, this is the first case so described.

Case Report

A 21-year-old primigravida had her last menstrual period on Oct. 4, 1953, with the estimated date of confinement July 11, 1954. There had been a history of painless vaginal spotting since her last menstrual period. The history was otherwise negative, and physical examination was negative except the findings of a six weeks' pregnancy. The patient was given progesterone because of her bleeding. She was a "Jehovah's Witness" and informed me that blood transfusions were contrary to her beliefs.

Later in November, 1953, there was one day of painless uterine bleeding which was treated conservatively.

The remainder of the pregnancy was normal up to the morning of June 29, 1954, approximately two weeks before the estimated date of confinement. The patient was hospitalized after an acute onset of painless vaginal bleeding estimated at 250 c.c. Immediately after admission, she began to have light uterine contractions.

Examination showed the patient to be in no distress. The blood pressure was 120/70 and pulse 84. The uterus was soft with irregular light contractions. The fetal position was right occipitoanterior with the head deep in the pelvis. The fetal heartbeat was regular, 144 per minute. Vaginal bleeding was mild, but continuous.

As is our routine, 1,000 c.c. of blood was ordered crossmatched before the patient was taken to the delivery room for a sterile vaginal examination to rule out placenta previa. However, the patient again reminded me that as a Jehovah's Witness she could not receive transfusions or plasma. This, of course, completely changed all routine measures, and it was decided that if the bleeding persisted, no matter what the diagnosis, cesarean section would be done immediately.

However, a sterile vaginal examination disclosed no placenta previa and after rupture of the membranes, the bleeding ceased and the patient went into active labor. The vertex was presenting in right occipitoanterior position and the head descended to a plus-one station. It was discovered during the examination that the patient had a bicornuate uterus. (In retrospect, I attribute missing this fact during the patient's office visits to the thought that the rounded protuberance in the right cornu was the breech.)

The patient continued in excellent labor and in three hours delivered a 7 pound, 3 ounce, normal boy with the aid of outlet forceps. As is our routine, the patient received Pitocin intramuscularly after delivery of the anterior shoulder. There was no third-stage bleeding. As soon as the uterus contracted, the bicornuate uterus was easily identified just by looking at the abdomen.

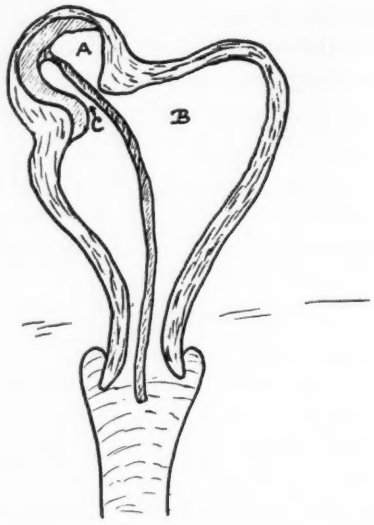

Fig. 1.—Schematic drawing showing bicornuate uterus. Placenta was implanted in right horn (*A*) with small edge of placenta and cord issuing through 3 cm. os into main cavity of uterus (*B*). Fetus was lying in main cavity (*B*) and delivered normally.

The placenta showed no evidence of delivering even with continuous uterine massage. After one hour, the patient was redraped and manual removal of the placenta was attempted. There was still no appreciable uterine bleeding.

On entering the uterine cavity it was immediately apparent that this was no routine manual removal of the placenta. Approximately 2 inches of placental lip was felt separated in the upper right corner of the main uterine cavity, but the cord and the remainder of the placenta disappeared through a 3 cm. os into the chamber of the rudimentary right horn. All one could do was to insert two fingers through this os and wave them around without even touching placenta or insertion of cord. Deep ether anesthesia did not relax the opening. A consultant could do no more than remove the small piece of placenta that was loose in the main cavity.

As the patient still was not bleeding, it was felt that, for the time being, we could be conservative and allow the placenta to remain in situ.

Here again, however, the fact that the patient refused transfusion completely dominated the method of treatment. Ordinarily she could have been watched with blood transfusion and antibiotic therapy, with final treatment conservative or radical as circumstances warranted. At a consultation, three possible results were considered:

1. The patient could pass the placenta spontaneously with no serious effects.
2. She could partially separate the placenta and bleed profusely, and, with our inability to give blood, would be a poor surgical risk.
3. The uterus would become infected after two invasions, she would then undoubtedly bleed, and would end up an even poorer surgical risk.

After deliberate discussion of these facts and the alternative of removing the uterus of a 21-year-old primipara, it was unanimously decided that immediate hysterectomy was in order.

Under ethylene and ether anesthesia a right paramedian incision was made and the uterus delivered externally. The right horn was a large, 15 cm., thin-walled organ on a broad base. Many veins of large diameter almost completely covered the serosal surface of the horn. The horn was not incised or excised because of the probability of hemorrhage. A total hysterectomy was done with a minimal loss of blood. The patient received dextran, a synthetic plasma, during the operation. The systolic blood pressure remained between 80 and 120.

Postoperatively the patient did very well although her color was a dead white. The red blood count was 2.4 million, hemoglobin 7.1 Gm. per cent, and hematocrit 26 per cent. The patient received massive hematinic therapy postoperatively. Four weeks after operation, she had done well with satisfactory response to the hematinics.

Summary

A case is presented of abruptio placentae complicated by incarceration of the placenta in a rudimentary horn of a bicornuate uterus. This case was further complicated by the patient's refusal to receive blood transfusions because of her religious beliefs. The treatment was a total abdominal hysterectomy post partum.

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PSYCHIATRIC MANAGEMENT OF A CASE IN WHICH TERMINATION OF PREGNANCY WAS RECOMMENDED BUT NOT DONE

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THIS case of rheumatic heart disease with pregnancy is presented because of the interesting psychological factors encountered.

The patient, a 20-year-old married white woman, was admitted as an emergency to the Presbyterian Hospital on April 8, 1948, because of attacks of shortness of breath complicating pregnancy. Her last menstrual period was Dec. 15, 1947, and although she had one attack of dyspnea when 17 years old, she was free of symptoms until January, 1948, when her family physician gave her injections to make her pass her water and prescribed a salt-free diet with restricted fluid intake. Since January, she had five attacks of dyspnea of increasing severity. She had slept on three pillows since January and had been unable to take more than five steps without shortness of breath. Headaches and cardiac palpitation were associated with pain radiating down the left arm. The last attack occurred on April 2, 1948, at which time she was admitted to a hospital and placed on oxygen therapy and sedation. She was discharged as improved after two days.

Past History.—When 12 years old, she had growing pains without swelling of the joints. No medication or bed rest was prescribed. Tonsils and adenoids were removed in childhood and an appendectomy performed when she was 19 years of age. Menstruation began when she was 12 years old. Cramps were present on the first but not the three remaining days, and the cycle was regular.

Family History.—Both the father and mother were living and well, and in their fifties. Three sisters and one brother were living and well. Four siblings had died from causes unknown to the patient. The husband was 22 years of age and worked as an attendant in a mental hospital.

Personal History.—She was the fourth of nine children. Her parents were of Spanish extraction and both worked to provide meagerly for their children. When the mother was four months pregnant with the patient, the second oldest daughter suddenly died. The mother became severely depressed and was unable to take care of the children. This had been told to the patient as an explanation of her poor health in childhood as well as her heart condition. Because the patient was weak and undernourished, she remained home from school after the sixth grade. She helped her mother and father knit articles which were sold to provide an income. For the past ten years, the father had worked as an attendant in a state hospital. He introduced her to one of the young hospital attendants who subsequently became her husband. Marriage was proposed shortly after the patient was refused employment because of a heart condition. She was told by the examining physician that she could have a baby only at a severe risk to her life. The husband was informed of this prior to marriage and the patient quoted him as saying that, although he loved children, he cared more for her and suggested they marry as soon as possible. The husband was of Catholic and the patient of Protestant faith and they were married in a Protestant church.

The family physician who made the premarital tests advised them to have a child at the earliest possible date because her heart would gradually become weaker and pregnancy a threat to her life. To check this opinion, he referred her to a cardiologist who advised against

pregnancy for at least one year. It was shortly after this and under the circumstances described that the patient became pregnant. During the first three months of pregnancy, she had almost constant vomiting and she was advised to enter the hospital to consider termination of pregnancy.

Physical Status.—On the admission examination, the patient did not appear in acute distress. There was a marked throb in the carotid vessels. The heart was enlarged to the left and down. There was a strong apical thrust and thrill throughout the precordium and a loud blowing systolic and a short diastolic murmur at the apex, and a marked blowing systolic and diastolic murmur in the aortic area. The murmurs were transmitted upward and to the left. The liver edge was 2 cm. below the costal margin and tender. The fundus was two fingerbreadths above the symphysis. The extremities showed no peripheral edema. The neurological examination showed no significant deviations.

The diagnostic impressions were: (1) pregnancy of three and one-half months' duration, and (2) rheumatic heart disease with mitral stenosis and not well compensated.

Laboratory Studies and X-rays.—The electrocardiogram showed left axis deviation with myocardial damage and changes due to the effects of digitalis. The x-ray impression was that cardiac enlargement was more suggestive of an aortic rather than a mitral lesion.

Psychiatric Examination.—When first seen, May 12, in consultation by the psychiatrist, the patient appeared tense and frightened. She said she had been feeling better since May 10, when she and her husband had both given consent to abortion and sterilization. She related the conflicting opinions regarding the advisability of pregnancy and that her husband had married her knowing that pregnancy was a danger to her life. She was assailed with fears and doubts during the first three months of pregnancy and was somewhat relieved by vomiting, which was almost constant. The attacks of shortness of breath recalled stories she had heard that pregnant women were unable to breathe as the baby grew larger and pressed on the lungs. She visualized this as a slow death. She quoted the admitting physician's opinion that she would be able to have her baby provided she remained in the hospital for the duration of her pregnancy. Since the patient's symptoms became more severe and her cardiac reserve depleted, it was decided that termination of pregnancy was indicated. The husband delayed consent on the basis of the conflicting opinions but agreed as her condition became more serious and she was placed on the critical list. When she was seen, shortly after this, by the medical consultant, he expressed the opinion that pregnancy was far advanced and the patient's cardiac reserve too small to risk the performance of an abortion, that it was advisable to carry the patient to term.

Course in the Hospital.—The patient was seen weekly for psychiatric interviews in which she freely expressed her resentment toward the staff and her husband for waiting until it was too late for the abortion. She responded to the medical consultant's recommendation by having frequent attacks of dyspnea, hot flushes with profuse perspiration, migratory chest and precordial pain, tachycardia, moaning, and severe anxiety. These symptoms were somewhat but not entirely relieved by Demerol and oxygen. She voiced no objection to the interpretation that her symptoms represented, in part, an unconscious attempt to interrupt her pregnancy. She expressed the fear that her baby if born would suffer a heart condition or be deformed. The basis for this fear was interpreted as being related to the feeling that she of necessity would go through the same experiences in pregnancy as her mother had undergone. She expressed hatred and distrust for her husband who had not visited her for the preceding two weeks and denied any connection between these feelings and her husband's refusal to consent to the abortion until it was too late. It was not until one week later that this connection was verified by a dream in which someone told her that her husband had been killed. She reacted to the emotional content of the dream with increased uterine contractions which necessitated her being taken to the labor room where she remained for twenty-four hours when the contractions subsided. Following this, she expressed more freely her hostility toward her husband and the hospital staff. Her attacks of dyspnea decreased after she experienced a hypnagogic hallucination of her grandfather

whom she had seen die while in an oxygen tent. The oxygen tent was discontinued and oxygen administered nasally when required. Another source of anxiety was resolved when the patient was permitted to decide whether she was to remain on the critical list as her medical condition no longer was classified as critical. On August 20 she was delivered of a normal baby under caudal anesthesia with low forceps. Her condition remained good and she was permitted out of bed August 29, but two days later developed a pulmonary embolus and her condition deteriorated, with a poor prognosis. She gradually responded to treatment and was well enough to be discharged from the hospital with a healthy baby one month later.

SACRAL TUMOR OBSTRUCTING LABOR

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THE subject of pelvic tumors of extragenital origin was exhaustively studied by Lovelady and Dockerty.[1] We wish to report a case of chondrosarcoma of the sacrum which obstructed the birth canal and which, unfortunately, was not recognized prior to labor, with a fatal outcome for the fetus.

Mrs. T. W. (78703), a white, 29-year-old gravida ii, para i, was first seen on May 5, 1953. Her past history disclosed an appendectomy at the age of 9 and a curettage for unknown reasons at an undetermined date. The menarche occurred at 12 years, with regular cycles and no dysmenorrhea. She had had what was reported to be a normal vaginal delivery of a full-term infant in October, 1951, in a distant community. Her last menstrual period was Aug. 25, 1952, and the expected date of confinement June 1, 1953.

She had been under the care of a physician in the community where she had previously been delivered, and it had been her intention to return to him for delivery. Labor began about 2 A.M. on May 5, 1953, however, and she was admitted to the hospital at 7:30 A.M. in active labor. She was first seen by one of us at 8:30 A.M., at which time rectal examination disclosed a fecal impaction which was manually removed, after which the cervix was found to be 3 cm. dilated, 70 per cent effaced, the vertex presenting at station 0. The fetal heart tones were of good quality and regular.

At 10:15 A.M., vaginal examination on the delivery table disclosed complete dilatation of the cervix, and a bony protuberance was palpated posteriorly, which was felt to encroach upon the birth canal, but which it was thought would not preclude vaginal delivery. Manual rotation from right occiput posterior to right occiput anterior was performed, and Simpson forceps were applied, but extraction was impossible. It was at this time that fetal heart tones began to fail, and consultation was requested. Examination now showed the cervix to be fully dilated, the vertex in left occipitoanterior position; fetal heart tones were absent. There was a very firm mass, apparently arising from the sacrum, which was estimated to be approximately 9 to 10 cm. in diameter, the anterior surface of which was round, and seemed to extend 7 to 8 cm. above the anterior surface of the sacrum. Rectal examination showed the rectum to be tightly stretched over this mass, but the rectal mucosa did not appear to be invaded by tumor.

Although the fetus was assumed to be dead, it was felt that it would be extremely dangerous to remove it per vaginam, and a low-flap cervical cesarean section was performed. The postoperative course was uneventful, and the patient was discharged on May 15, 1953. Prior to discharge from the hospital, x-ray examination showed a tumor mass located on the anterior wall of the lower half of the sacrum, with considerable destruction of the anterior wall of the sacrum. The mass measured 6 cm. in width, 7 cm. in length, and 6 cm. in thickness. The roentgenologist considered the mass to be probably a chondroma. The other bones of the pelvis were of normal appearance. An opaque enema filled the colon completely and well. The lower portion of the sigmoid flexure of the colon was deviated about the sacral mass, but showed no encroachment on the lumen. Chest films showed no evidence of primary or metastatic lesions.

On June 3, 1953, the patient was admitted to the Memorial Center for Cancer and Allied Diseases in New York City. At this time she had no complaints with the exception of moderate constipation. After further study, on June 15, 1953, the patient had a local excision of the tumor and adjacent sacrum performed by Dr. Bradley Coley. Bladder and bowel atonia gradually improved, and the patient was discharged on July 17, 1953, with a final diagnosis of chondrosarcoma of the sacrum.

Twelve months after delivery, and approximately ten months after removal of the chondrosarcoma, the patient feels well and has regular menses. She has no bladder disturbance, but suffers from constipation which is relieved by citrate of magnesia. There has recently been slight drainage from the upper angle of the incision over the sacrum. The uterus and adnexal structures are normal, and no recurrence of the sacral tumor is apparent.

Comment

Unfortunately, this patient was not seen until she was in active labor. Failure to recognize immediately the insurmountable obstructing tumor of the sacrum resulted in the death of the infant. It may be assumed that this tumor was either not present, or very small at the birth of her first child in October, 1951. A communication from her former physician informs us that he detected no pelvic tumor when diagnosing her first pregnancy, and that this was terminated without difficulty with a low forceps application. Marked constipation was a feature of both pregnancies. No pelvic examination was made at any of the four prenatal visits of the second pregnancy.

Reference

1. Lovelady, S. B., and Dockerty, M. B.: Am. J. Obst. & Gynec. 58: 215, 1949.

Department of Reviews and Abstracts

EDITED BY LOUIS M. HELLMAN, M.D., BROOKLYN, N. Y.

Review of New Books*

Fat Metabolism: A Symposium on the Clinical and Biochemical Aspects of Fat Utilization in Health and Disease. Edited by Victor A. Naajar. 185 pages. Baltimore, 1954, The Johns Hopkins Press. $4.50.

This is a collection of ten papers, with discussions by five of the participants. Four papers (counting discussions) deal with obesity, from the clinical, experimental, and speculative aspects. In this section there is an excellent review of the "glucostatic mechanism of regulation of food intake"—when the arteriovenous difference in blood sugar (Δ-dextrose) falls below 10 mg. per 100 ml., hunger is felt and hunger contractions of the stomach occur. Obese subjects take up dextrose rapidly following meals, and show a large Δ-dextrose for a short period. The Δ-dextrose then falls rapidly and hunger recurs.

Mayer reported some very interesting studies of obesity in mice. Young, genetically obese mice were pair-fed with controls and the incorporation of radiocarbon acetate into body lipids measured. The obese animals stored far more labeled lipids, both in the carcass and the liver, than did the controls. Similar experiments were done with mice that had gold thioglucose obesity and hypothalamic obesity. In the former, the test and control animals retained almost identical amounts of labeled lipids, while in the latter the test animals stored carcass fat in excess but showed no difference from the controls in liver fatty acids.

Other topics include two papers on hyperlipemia, one on the preparation and use of neutral fat emulsions for intravenous administration, and one on the relation of the lipemia-clearing factor to lipid transport. Lipmann brilliantly reviewed the role of coenzyme A in fat metabolism and Zehninger the enzymatic oxidation and synthesis of fatty acids. Bessman suggested that the enzymatic "lesion" in diabetes may be the failure to phosphorylate dextrose through the hexokinase reaction. Gurin reviewed some fascinating work on the synthesis of fatty acids by the liver: the failure to utilize dextrose (insulin deficiency) involves the attendant lack of glycolytic intermediates necessary for lipogenesis. This could account for the ketosis and increased cholesterol synthesis. The last two papers deal with phospholipid and cholesterol metabolism.

This book gives a broad review of recent work on fat metabolism and can be recommended on this basis. It may be somewhat alien to the obstetrician, for the only mention of pregnancy is its listing in a table classifying the lipemias. The book is well printed and clearly legible. While typographic errors are inevitable, the repeated adjectival spelling "phosphorous" for the noun "phosphorus" does seem inexcusable.

Gynaecology for Senior Students of Nursing. By John Cairney. 211 pages with 71 illustrations. Christchurch, New Zealand, 1954, N. M. Peryer Limited. $5.25.

The book is well organized, comprehensive, and concise—a text that every nurse and student nurse will find invaluable in work and study. It reviews not only the latest procedures of gynecological surgery but also the anatomy, physiology, diseases of the reproductive system, and surgical aspects of gynecological nursing.

*The Advisory Committee on Policy has agreed that most book reviews need not be signed.

The diagrams are masterpieces of visual instruction because they are self-explanatory. The simplified terminology provides for easier and more interesting reading.

Diagnostik und Strahlentherapie der Geschwulstkrankheiten. By Alfred Vogt. 382 pages with 209 illustrations. Stuttgart, Germany, 1955, Georg Thieme Verlag. $17.50.

This volume of 380 pages is not a textbook of radiation therapy as the title would suggest. Discussions of radiation technique, consideration of dose measurement systems, discussions of modern tissue-dose calculation are all prominent by their absence. In fact, old errors such as the confusing of Gamma R of radium and Roentgen R of x-ray crop up throughout the book. Neither is this a textbook of diagnosis and classification of the clinical pathology of cancer. Discussions of pathological histology are largely omitted. The diagnosis of early carcinoma is inadequately treated. This volume is essentially a conducted tour through the realm of cancer, touching upon the well-known guideposts and established concepts of the field. As such, it is recommended to the general practitioner who wishes to review this currently vital speciality in a broad and general way without burdening himself with any amount of technical or statistical detail.

The author leans very lightly on his own experience, and very heavily on past literature. There are over a thousand quotations or references to the literature. This would imply a considerable scholarship, but unfortunately the selection of references and quotations includes many past publications that are no longer fully accepted. There are also some obvious errors. On page 88 is the statement that breast carcinoma was first treated by x-ray in 1887 by Gocht, a most amazing reference antedating the discovery of x-ray by several years. On page 86 the author states that only rarely bleeding from the nipple is not associated with carcinoma of the breast. The general American statistics place the incidence of breast carcinoma with bleeding nipples at approximately 60 per cent. The author recommends the use of preoperative radiation in breast carcinoma and fails to state the tumor dose he requires. On page 95 the statement is made that the diet of women with cancer of the breast should be fat free and rich in vitamin B. These and other such generalizations weaken the significance of the book. Cure rates are stated without statistical analysis. Some of those claimed are hard to accept at face value. For instance, the author claims 56 per cent five-year cures of urethral carcinoma by radium alone. On page 135 the statement is made that the cosmetic result in carcinoma of the skin treated by radiation is always better than that of surgery. Further in the book the author recommends preoperative radium therapy for melanosarcoma, a notably radiation-resistant tumor. In the discussion of Schmincke tumors (pages 149-154) no mention is made of skull base erosion and cranial nerve involvement, a usual presenting syndrome.

The illustrations are well reproduced but consistently demonstrate advanced lesions and therefore are, as is most of this volume, far behind the current needs. The German text is easily readable. The volume is beautifully printed.

Genetica Medica. Edited by Luigi Gedda. 467 pages. Rome, 1954, Gregorio Mendel.

Papers presented at the First International Symposium on Medical Genetics in Rome, in September, 1953, compose this volume. It is, therefore, not a systematic or complete treatise of medical genetics. There are thirty articles in Italian, English, German, or French; many of them include translations of the summary in the remaining three languages. Such divergent subjects an anemias, mental and endocrine disorders, skeletal abnormalities, deviations of metabolism, and others are represented. Investigations of identical twins are reported in many of the papers. An extensive address of Pope Pius XII is printed in four languages.

Gynäkologische Rontgendiagnostik. By Gunter K. F. Schultze and Joachim Erbelch. 396 pages with 239 illustrations. Ferdinand Enke Verlag. Stuttgart, Germany, 1954, DM 59.

In the first part of the book the authors described the normal variations of the uterus, the cervix, and the Fallopian tubes when visualized by x-ray following the instillation of a contrast medium. For most of the studies the contrast media were Iodophin and Lipiodol. The course of the opaque material was followed under fluoroscopy. The pressures were regulated according to the reading on a manometer which had been previously attached to the injecting apparatus. The potential dangers of hysterosalpingography and the possible harmful effects from its improper or careless use were cited.

In the second part of the book the pathological lesions of the uterus and Fallopian tubes as seen by hysterosalpingography were discussed. The appearance of the roentgenographic shadow in uterine hypoplasia, congenital uterine anomalies, and uterine malposition was described and illustrated. The section of the book on the use of hysterosalpingography to aid in the differentiation of the causes of uterine bleeding was well presented. The uteri of some women in early pregnancy were filled with contrast media. The findings were illustrated by roentgenograms. Pathologic alterations of the Fallopian tubes which occurred at the interstitial, isthmic, and ampullary region as seen on x-ray were reported. The discussion of cervical pathology, as seen on x-ray with the use of contrast media, was short and inadequate.

In general, however, the book was a well-documented analysis of the subject of hysterosalpingography. The roentgenograms were excellently reproduced and the printing was good. The book should be a valuable reference for those who perform hysterosalpingography and can read German.

Practical Obstetrical Problems. By Ian Donald. 578 pages. Chicago, 1955, The Year Book Publishers, Inc. $9.50.

This text correlates basic obstetrical knowledge and the present-day application of some of these fundamental principles. In not too many years theories of management of the problems in this field have progressed markedly, producing, however, some confusion as to which practices are correct, need improvement, or are to be discarded. The author expresses rather definite opinions concerning complicated pregnancy.

The scope of the book is impressive. In 29 chapters the author has considered antenatal and postnatal care, diabetes, cardiac disease, hemorrhage, prematurity and postmaturity, Rh factors, and other topics. Contributors have added information on antibiotics, pain relief, toxemias of pregnancy, and abnormal presentations.

The facts presented are frequently emphasized by the personal experiences of Professor Donald. Occasionally the material is directed at the midwife rather than the physician. Unfortunately, those situations requiring the assistance of a "flying squad" have to be handled differently in most areas in the United States.

References are made to recent contributions by other investigators of specific obstetrical problems. A brief bibliography follows each chapter. The illustrations include good photographs and fair drawings. The index is valuable. In general this volume, although not the final word, is worth-while reading.

Selected Abstracts*

Geburtshelfe und Frauenheilkunde

Vol. 14, No. 5, May, 1954.

Brandl and Grünberger: Value of Different Special Examinations in Diagnosis of Suspicious Erosions of Cervix, p. 443.

Cervical erosion, in many cases, may be the precursor of carcinoma. In the examination of 2,000 cases, lesions resembling erosion of the portio were noted in approximately 10 per cent of all women studied. In all of these, it was necessary to establish definitely the presence or absence of early malignancy. To evaluate the lesions, four special procedures were carried out on each case, the final diagnosis being made by actual biopsy and section. In 170 cases, the following procedures were studied: (1) vaginal cytology (Papanicolaou); (2) colposcopy (Hinselmann); (3) colpomicroscopy (Antoine and Grünberger); and (4) histological examination of tissue removed by a high-frequency current scalpel. Each examination was done by a different individual, and results compared with the actual histological picture. Cases were divided into negative, suspicious and positive categories. In general, the study of the vaginal cytology gave more suspicious and positive results than did either of the two other methods studied. Furthermore, a greater degree of coordination was found with cytological studies than with the other special tests, when compared with the biopsy technique. None of the methods, cytology, colposcopy, or colpomicroscopy, equals the accuracy of diagnosis by biopsy in differentiating nonmalignant erosions of the cervix from true malignancy, although the cytological method of Papanicolaou most closely approached it.

L. B. WINKELSTEIN, M.D.

Edinburgh Medical Journal

Vol. 61, June, 1954.

Brown: Contracted Pelvis, p. 181.

This is the Honyman Gillespie Lecture delivered in Edinburgh, June 18, 1954, being a review of the experience with contracted pelvis at the Simpson Maternity Pavilion for the years 1950-1951.

DAVID M. KYDD, M.D.

*Titles preceded by an asterisk are abstracted below.

Vol. 61, August, 1954.

*Hobson, B. M.: The Routine Diagnosis of Pregnancy, Hydatidiform Mole and Chorionepithelioma Using Female Xenopus Laevis, p. 33.

*Rolland, Charles: Diabetes in Pregnancy, p. 257.

Hobson: Routine Diagnosis of Pregnancy, Hydatidiform Mole and Chorionepithelioma Using Female Xenopus Laevis, p. 33.

The University of Edinburgh Pregnancy Diagnostic Laboratory, now 25 years old, deals with 25,000 tests each year. In this laboratory all the estimations are done upon the female South African clawed toad—*Xenopus laevis.*

The amount of chorionic gonadotrophin present in a positive injection of urine is said to be related to the number of eggs a toad lays. A weakly positive or negative biological reaction from what seems to be a normal pregnancy may be a warning sign.

The prime necessities of any biological test are accuracy and specificity. In a series of tests done between January, 1949, and June, 1951, 15,000 Aschheim-Zondek tests gave a correct result in 99.5 per cent of the cases and 37,000 Hogben tests resulted in an accuracy of 99.8 per cent.

Aside from the many pregnancy tests, the Diagnosis Laboratory does about 1,000 dilution tests a year. These tests are requested when a pregnancy is not behaving normally, or a hydatidiform mole or chorionepithelioma is suspected. The test is similar to the pregnancy test except that the urine or concentrate is diluted with distilled water before injection. Observations of Zondek (1929) and Aschheim (1930) showed that women with hydatidiform moles excrete abnormally large amounts of chorionic gonadotrophin. If a test is positive in a dilution of 1/100, further dilutions are done until no positive response is obtained. Work done in the Diagnosis laboratory shows that a positive reaction in a dilution of 1/100 or more is given in 48 per cent of molar cases, 35 per cent of chorionepitheliomas, and 6 per cent of normal pregnancies. Positive reactions in high dilutions obtained after the fourteenth week of pregnancy are more reliable, the peak of excretion of gonadotrophin in normal pregnancy having passed. Dilution tests are especially significant in the follow-up after removal of a mole or epithelioma. It seems to be advisable to do weekly tests for the first month, followed by monthly tests for the next six months. The biological tests would show an increasing gonadotrophin output and would allow for treatment at an earlier date than if the clinician waited for a definite clinical sign.

M. J. Fitzpatrick, M.D.

Rolland: Diabetes in Pregnancy, p. 257.

This is the Honyman Gillespie Lecture delivered in Edinburgh, May 14, 1953, being a report of 77 pregnancies in 64 diabetic women. There was no maternal mortality. The fetal death rate was 28.6 per cent. Three spontaneous and two therapeutic abortions occurred. The latter were performed for vascular complications of the diabetes. There were 9 instances of intrauterine death, cause unknown; 2 stillbirths (neither baby was of exceptional size); and 5 neonatal deaths. The author briefly reviews what is known of the prediabetic state and hormonal influences. Values of chorionic gonadotrophin in the serum and urine obtained after the hundredth day are reported. He found that high values in any one individual were of no prognostic significance with regard to the fate of the fetus. Serial pregnanediol estimations were reported also, but again no correlation was found with the outcome of the pregnancy. The author has not found that the administration of stilbestrol or progesterone has any influence on the fetal mortality rate. No relationship was demonstrated between the length of time the mother had had diabetes and fetal mortality. The author believes that early delivery by cesarean section may save some babies. He comments on the difficulties encountered in controlling diabetes mellitus in pregnant women.

David M. Kydd, M.D.

Vol. 61, September, 1954.

Irving, Patterson, and Myerscough: Symposium on Caesarian Section. Part I. General Review: Indications for Operation and Type of Operation, p.39.

The survey includes 1,796 cesarean sections carried out on 1,612 women. During the decade 1940-1950 there has been a small increase in the incidence. In about half the cases there was a single indication for the operation while in the remaining half a combination of several factors created the indication. The authors have noted an increasing tendency during the decade to justify the decision to operate by a summation of indications when each individual indication is not sufficiently strong to warrant the decision. Dystocia (39 per cent), hypertensive toxemia (17 per cent), disordered action of the uterus (12 per cent), and hemorrhage (11 per cent) were the chief indications. Forty-five per cent were delivered by classical cesarean section. There has been a slow trend toward the lower segment operation but only in disordered action of the uterus and contracted pelvis is there a marked predilection for this type of operation. The extraperitoneal cesarean section was performed in only three cases which were not grossly infected.

DAVID M. KYDD, M.D.

Adamson: Symposium on Caesarian Section. Part II. Maternal Mortality and Morbidity, p. 48.

The maternal mortality was 1 per cent (18 deaths following 1,796 operations). During the first five years of this decade, however, the mortality was 1.8 per cent, while during the second five years it was but 0.5 per cent. There were no deaths from pulmonary embolism. There was a high mortality from the operations performed on patients with cardiac failure (16 per cent of 25 cases). Three patients died from the results of hemorrhage and 2 from peritonitis. All of these latter deaths occurred early in the decade. Of 126 patients who had been in labor more than forty-eight hours, 4 died. (One died from peritonitis, 2 from postoperative shock, and one from dilatation of the stomach.) Of 13 patients with eclampsia 2 died, which is contrasted with the mortality rate of 7.3 per cent in patients with eclampsia delivered by the vaginal method. Concerning the two chief types of operation, the authors feel that maternal mortality has reached so low a figure that it cannot be used as an index of worth of either operation. Concerning morbidity, there has been a decrease in serious infections due to the use of antibiotics, but more than 13 per cent of the cases in the second half of the decade were still complicated by fever.

DAVID M. KYDD, M.D.

Dunlop: Symposium on Caesarian Section. Part III. Stillbirth and Neonatal Mortality, p. 54.

The perinatal mortality rate was found to be 11.1 per cent (stillbirths 3.8 per cent and neonatal deaths 7.3 per cent). There has been very little change in this rate during the last eight years of the decade. Of the stillbirths, 40 of the 68 instances were reported as being due to asphyxia. Inasmuch as the autopsy rate was only 30 per cent,

these figures are of little value. So far as the neonatal deaths are concerned, 70 of 133 instances were reported as due to prematurity. Infections (15.8 per cent) and congenital malformations (8.3 per cent) were the other two prevalent causes of death. Relating stillbirths to the indications for the cesarean section, the authors found three important groups where improvement in mortality might be possible: (a) There were 6 stillbirths due to hydrocephalus, which should have been diagnosed before operation. (b) Twelve of the 15 instances of placenta previa were in "unbooked" patients. A suspicion of the condition would have obviated unfortunate delay. (c) In disordered uterine actions the labor was prolonged to more than 60 hours, and 4 of the 6 stillbirths occurred in multiple pregnancy. Concerning the relation of indications for operation and neonatal deaths, severe toxemia and placenta previa are associated with the largest number of deaths (39 per cent and 19 per cent of the total, respectively). All the other causes are of less importance because of the small numbers involved. Recent conservative policy in dealing with placenta previa advocated by Macafee has led to a lessened incidence of prematurity and lessened neonatal death rate.

DAVID M. KYDD, M.D.

Obstetrics and Gynecology

Vol. 4, No. 1, July, 1954.

Falk and Bunkin: Ureteral Injuries: Prevention and Management During Gynecologic Surgery for Benign Disease, p. 4.

The author of this paper points out that one would expect a rise in the number of ureteral injuries at the time of surgery to be concomitant with the increased volume of pelvic surgery that is being done today. A brief summary of the American literature, however, shows no such trend.

In the first half of the article there is an anatomical description of the pelvic ureter and its relationship to the pelvic peritoneum. The usual type of displacement of the ureter in the presence of various pathological processes is described.

The second part of the paper is given to the recognition and management of the usual types of injury. The authors' own statistics in over 6,000 gynecologic cases are cited.

THOMAS SULLIVAN, M.D.

Vol. 4, No. 5, November, 1954.

MacMahon, Brian, Hertig, Arthur, and Ingalls, Theodore: Association Between Maternal Age and Pathologic Diagnosis in Abortion, p. 477.

Zondek, Bernhard, and Cooper, Kenneth: Cervical Mucus in Pregnancy: Inability of Estrogen to Produce Arborization in Pregnancy and Its Clinical Significance, p. 484.

Reeves, Clyde P., and Savarese, M. F. R.: Simultaneous Intra- and Extrauterine Pregnancies: Report of a Case, p. 492.

Hofmann, J. W., and Atlas, J.: Cesarean Sections at Indianapolis General Hospital, p. 496.

Scott, Roger B., and Te Linde, Richard W.: Clinical External Endometriosis: Probable Viability of Menstrually Shed Fragments of Endometrium, p. 502.

Flanagan, James F., and Walsh, Charles R.: Cervical Pregnancy: Report of a Case, p. 511.

Cochran, Robert B.: Interstitial Pregnancy: Report of a Case, p. 514.

Riva, Humbert L., and Harding, Robert L.: Vaginal Reconstruction, p. 517.

Arje, Sidney L., and Bachman, Kenneth B.: Disseminated Lupus Erythematosus and Pregnancy: Report of a Case, p. 524.

Foraker, Alvan G., Denham, Sam Wesley, and Mitchell, Dorothy D.: Dehydrogenase Activity: III. In the Rabbit Placenta, p. 527.

Marbach, A. Herbert, and Schinfeld, Louis H.: High-Frequency Electrosurgical Vulvectomy: A New Technic, p. 536.

Godsick, William H., and Baydoun, Adnan B.: Adrenal Tumors of the Ovary (Masculinovoblastoma): Report of a Case, p. 542.

Roberts, Chester L.: Intravenous Caffeine in Prevention of Neonatal Asphyxia and Narcosis, p. 545.

Laufe, Leonard E., and Meyers, Louis L.: Mixed Mesodermal Tumors of the Uterus, p. 548.

Staples, Pelham P., Jr., and Riva, Humbert L.: Maternal Osteogenesis Imperfecta: Report of Two Cases in Sisters, p. 557.

Rosenfeld, Samuel S., and Bergman, Harry: Prevention of Urologic Complications From Injuries in Gynecologic Surgery, p. 562.

Burgess, Gordon F., and Shutter, Harold W.: Malignancy Originating in Ovarian Dermoids: Report of Three Cases, p. 567.

Lang, Warren R., Scheffey, Lewis C., and Farell, David M.: Delay Period in Diagnosis of Carcinoma in Situ of the Uterine Cervix: Observations From Collected Data of the Philadelphia Committee for the Study of Pelvic Cancer, p. 572.

Journey, R. Wallace, Gold, Herman, Wyman, Newton A., and Campbell, William N.: Unusual Complications of Cervical Cancer: Uremia and Alkalosis Due to Gastric Metastasis; Report of a Case, p. 575.

Stephenson, Henry A.: Therapeutic Abortion, p. 578.

Raftery, A., and Payne, W. S.: Condyloma Acuminata of the Cervix, p. 581.

British Medical Journal

Vol. 2, July 10, 1954.

*Parker, R. B.: Risk From Aspiration of Vomit During Obstetrical Anaesthesia, p. 65.

Lesser, M., and Eason, G. A.: Cardiac Arrest Under Anaesthesia During Induction Of Labour With Pitocin Drip, p. 79.

Parker: Risk From Aspiration of Vomit During Obstetrical Anaesthesia, p. 65.

This article begins with a brief review of the cases of this unfortunate accident reported to date. The author states that Mendelson in 1946 divided aspiration of stomach contents into two groups, inhalation of solid material and the asthmatic type or aspiration of gastric secretions. Seven cases which occurred in the Birmingham Maternity Hospital are summarized. This hospital admits 50 per cent of its patient load in emergency status. In the ten-year period considered, 5 per cent of the maternal deaths may be attributed to aspiration during anesthesia.

The first case reported was one of the obstructive type and the treatment should have been immediate removal of the foreign body. The remainder of the cases were of the asthmatic type. These probably occurred during the induction phase of anesthesia when the reflexes were being eliminated by the gases. This results in laryngeal irritation and tracheitis and since the patient remains unconscious the acid substance spreads deeper along the respiratory tree. During recovery from anesthesia spasm of the bronchioles produces local areas of lung collapse. The acid aspirations also cause edema of the lung tissues.

Dr. Parker then reviews types of anesthesia applicable to operative obstetrics and selects local anesthesia as the safest. To prevent this mishap he advises taking no solid food after the onset of labor and limits to a minimum liquid feeding at this time. In conclusion he outlines treatment after the aspiration has occurred.

ARTHUR PERELL, M.D.

Vol. 2, July 17, 1954.

Walker, William, and Murray, Sheilaugh: The Management of Haemolytic Disease of the Newborn, p. 126.

Kimbell, Norman: Intramuscular Ergometrine and Hyaluronidase in Prevention of Postpartum Hemorrhage, p. 130.

Chalmers, J. A.: Torsion of Puerperal Uterus With Red Degeneration of a Fibromyoma, p. 138.

Vol. 2, July 31, 1954.

Moore, H. C.: Incoagulability of Blood After Accidental Haemorrhage, p. 277.

Vol. 2, Aug. 7, 1954.

Pike, L. A., and Dickins, A. M.: ABO Blood Groups and Toxaemia of Pregnancy, p. 321.

Vol. 2, Sept. 4, 1954.

MacFarlane, J. C. W., and Norman, A. P.: Serum Antithrombin Content in Pregnancy, p. 573.

Vol. 2, Sept. 11, 1954.

Hadfield, Geoffery: The Dormant Cancer Cell, p. 607.

Vol. 2, Sept. 18, 1954.

Barnett, Vivian H., and Cussen, C. A.: Acquired Afibrinogenaemia Complicating Pregnancy, p. 676.

Ellis, M. R.: Inversion of the Uterus, p. 686.

Laycock, H. T.: Advanced Ectopic Pregnancy Without Complications, p. 688.

Vol. 2, Oct. 2, 1954.

*Way, Stanley: Results of a Planned Attack on Carcinoma of the Vulva, p. 780.

Sandler, Bernard: Recovery From Sterility After Mumps Orchitis, p. 795.

Way: Results of Planned Attack on Carcinoma of Vulva, p. 780.

Attempting to improve upon the technique of surgical attack on carcinoma of the vulva, the Royal Society of Medicine in 1939 decided that it would be a valuable test to concentrate their studies in a few larger centers of medicine where teams could be trained and organized to develop methods of handling this problem. Dr. Stanley Way, the author of this article, was able personally to perform the surgery and direct the hospitalization of a large number of cases. This report covers the patients entering his clinics prior to March 31, 1949.

Briefly, the operation he performs is a radical vulvectomy with node dissection. He attempts to achieve a complete removal of the vulva from anus to mons down to the pubic bones and muscle; an excision of wedges of skin from the groin and saphenous region with the adjacent lymph nodes en bloc; the division of the inguinal ligament; and lymph node dissection to the bifurcation of the common iliac.

The author describes his results in table form. His operability rate was 83 per cent of 79 patients. The reasons for rejection of thirteen of the 79 cases are tabulated. The age distribution is similar to that in other published series of vulvar cancer. The absolute five-year survival rate was 61 per cent. Of the 65 operative cases, 44 had no involvement and 21 had invasion of nodes. The five-year survival rates for these two groups were 86 per cent in the former and 48 per cent in the latter.

To determine lymph node involvement at the time of surgery the rapid node-smear technique of Dr. Ruth Dearing was utilized.

The author states that he believes that the encouraging results of his clinic substantiate the value of this experiment and he recommends the plan to other centers.

ARTHUR PERELL, M.D.

Schweizerische medizinische Wochenschrift

Vol. 84, No. 29, July 17, 1954.

Keller, M.: Serial Study of Thromboembolic Phenomena in Gynecological and Puerperal Cases With Physico-chemical and Coagulation Physiological Methods, p. 810.

Western Journal of Surgery, Obstetrics and Gynecology

Vol. 62, August, 1954.

Bowles, H. E.: Compound Presentation of Brow, Foot and Hand at Term, p. 428.
*Duvall, Evelyn Millis: The Physician as Marriage and Family Counselor, p. 443.
*Rutherford, Robert N.: Prematurity Versus Immaturity Versus Maturity, p. 454.

Duvall: Physician as Marriage and Family Counselor, p. 443.

Appearing in the Professional Letters section of the *Western Journal of Surgery, Gynecology and Obstetrics* is Part III of a new volume, *From Family Counseling in Medical Practice,* by Evelyn M. Duvall, Ph.D., and Nadina R. Kavinoky, M.D. Part I of the monograph appeared in the July, 1953, issue.

The author in Part III re-emphasizes the role of the physician as a recognized professional confidant. She defines "counseling in general as a process wherein an individual (or a group) talks through a problem he is facing with a second person in whom he has confidence in the hope of gaining understanding of his difficulty, insight into himself, some clearer sense of direction, and more effective mobilization of his resources than he has had, so that he may face the future with more adequate health, and make decisions with greater maturity and well being."

She quotes the study of 2,566 consecutive cases at the Marriage Council of Philadelphia broken down for the following primary indications for marriage counseling.

General Preparation for Marriage in 23.0 per cent; Specific Marital Problems, 16.0 per cent, and Problems of Married Persons, 61 per cent. In the second group illegitimate pregnancy was the problem in about 1 per cent of the cases, while in the third group sexual difficulties was the opening problem in 15.0 per cent.

The author gives an excellent outline of the formulation of common concepts in marriage counseling practice. She evaluates the physician's assets and liabilities and limitations as a marriage and family counselor. The principal handicap of the physician is the very authority he has just by virtue of being a physician, i.e., "The doctor knows all the answers and will perform a cure." It is understandable that some doctors exploit this role to the detriment of their practice and professional skill. Too, the pressure of time is one of the greatest limitations to the physician's acting as a counselor. Most doctors do not have time to "hear out" the presenting problems.

The author then discusses Inservice Training essential to becoming an adequate counselor and she stresses that there should be rigorous courses, supervised clinical practice, and critical evaluation of one's efforts. She emphasizes the negative also encountered by the limits of overspecialization—the "pass-the-buck" weakness of overspecialization which operates as a disservice to both the physician and patient. She concludes this part of her book with a summary of fundamental questions about marriage and family counseling.

CLAIR E. FOLSOME, M.D.

Rutherford: Prematurity Versus Immaturity Versus Maturity, p. 454.

Rutherford points out that one of the most perplexing problems confronting us in present-day obstetrics and pediatrics is whether the baby is mature or not. His "twelve-baked potato" analogy is well taken and should be read by all obstetricians.

The author stresses the many new pediatric physiological problems we as obstetricians present to the succeeding pediatrician as related to prematurity, immaturity, and maturity of the infant. The author concludes his cogent editorial with the plea to obstetricians that we as well as pediatricians should remain alert to all new progress in this new phase of neonatal physiology. Obstetricians could aid by being more precise in their information relevant to degree of maturity of the infant whenever possible, for only in such a manner can we provide the pediatrician with a better product.

CLAIR E. FOLSOME, M.D.

Vol. 62, September, 1954.

Roe, William F., and Berne, Clarence J.: The Effect of Adrenalectomy and Oophorectomy in the Treatment of Far Advanced Carcinoma of the Breast, p. 457.

*Berger, Knute: No Spitballs, Sir Astley? p. 498.

Berger: No Spitballs, Sir Astley? p. 498.

In the section on Professional Letters the author dwells in a humorous and whimsical manner upon a most important subject—How not to give a scientific paper.

He concludes that speakers should (1) get to the point and be brief, (2) give essential principles to permit understanding, and (3) talk to the audience, *not* the subject matter. In these days of increased number of national and regional conferences this valuable paper should be familiar to all speakers concerned with presenting scientific articles before an intelligent and professional audience. This article should be *required* reading for all obstetric and gynecologic residents; perhaps then in two to three more decades we would have more interesting scientific meetings.

CLAIR E. FOLSOME, M.D.

Vol. 62, October, 1954.

*Duvall, Evelyn Millis: Implications of the Developmental Tasks for Counseling, p. 543.

Duvall: Implications of the Developmental Tasks for Counseling, p. 543.

The author concludes the last of four articles summarizing her book, *Family Counseling in Medical Practice.* She stresses how the physician is in a peculiarly favorable counseling position since he enters the patient's life at most of the crisis points, birth, sickness, marriage, pregnancy, parenthood, adolescence, the climacteric, and senility. She states that a developmental task is defined as a growth responsibility that arises at or about a certain period in the life of the individual, the successful achievement of which leads to his happiness, well-being, and success with later tasks while failure leads to unhappiness and distress of the individual, disapproval of society, and difficulty with later tasks.

She states that the origin of the individual's developmental tasks are three: (1) physical maturation; (2) cultural pressure; and (3) personal values and aspirations. She then proceeds to outline these for an individual from birth to middle age, using the following main categories: (1) the infant child, (2) the preschool child, (3) the school child, (4) the teen-ager and young adult, (5) the recently married couple, (6) the parents of young children, (7) the parents of school-age children, and (8) the parents of adolescents.

The article is well written and the ideas it leaves are most helpful to the thinking man in our specialty who professes to take a true human as well as professional interest in his patients.

CLAIR E. FOLSOME, M.D.

Journal of Clinical Endocrinology and Metabolism

Vol. 14, No. 8, August, 1954.

*Arnold, A.: Effects of X-irradiation on the Hypothalamus, p. 859.

*Kinsell, L., Bryant, D., and Albright, F.: Rate of Growth of Axillary Hair as a Diagnostic Index, p. 897.

Arnold: Effects of X-irradiation on Hypothalamus, p. 859.

Irradiation to the hypothalamic area of adult monkeys was done to determine the histologic changes. Following irradiation the monkeys were sacrificed at varying intervals and the brains examined. There was marked degeneration of the paraventricular and supraoptic nuclei of the hypothalamus. Since these nuclei exert a considerable influence on the function of the pituitary body and since the latter is relatively radioresistant, the authors suggest that any therapeutic benefits following x-irradiation to the hypophyseal region may occur because of the effects of x-rays upon the hypothalamus.

J. EDWARD HALL, M.D.

Kinsell, Bryant, and Albright: Rate of Growth of Axillary Hair as Diagnostic Index, p. 897.

The authors attempted to show a correlation between the rate of increase in axillary hair mass and the urinary 17-ketosteroid excretion. The seasonal factor had to be considered since there was a greater rate of growth during June and July. The authors assume that the rate of growth of the axillary hair is dependent upon two endocrine glands; the adrenal cortex and testes. Since, however, the function of the adrenal cortex is dependent upon the normal function of the anterior pituitary, any disturbance of the latter will influence the function of the adrenal cortex. In normal individuals, variations in the rate of growth of axillary hair are not closely correlated with similar individual variations in the urinary 17-ketosteroid excretion. Conditions associated with absence or extreme decrease of urinary 17-ketosteroids, however, are characterized by a comparable absence or decrease of axillary hair growth.

J. EDWARD HALL, M.D.

Vol. 14, No. 9, September, 1954.

Burt, A. S., and Velardo, J. T.: Cytology of Human Adenohypophysis as Related to Bioassays for Tropic Hormones, p. 979.

Wayne, H. L.: Convulsive Seizures Complicating Cortisone and ACTH Therapy: Clinical and EEG Observations, p. 1039.

Vol. 14, No. 10, October, 1954.

*Hisaw, F. L., Velardo, J. T., and Goolsby, C. M.: Interaction of Estrogens on Uterine Growth, p. 1134.

Finkler, R. S.: Acromegaly and Pregnancy: Case Report, p. 1245.

*Klinefelter, H. F., Jr., and Jones, G. E. S.: Teaching Clinic: Amenorrhea Due to Polycystic Ovaries, p. 1247.

Hisaw, Velardo, and Goolsby: Interaction of Estrogens on Uterine Growth, p. 1134.

The authors have attempted to show the different effects of estradiol, estrone and estriol on the growth of the uterus in castrated rats. The most marked growth followed the administration of estradiol, and estrone was about one-tenth as effective. Estriol produced very little uterine growth and if given with either of the other estrogens, inhibited their effectiveness.

Estriol is the predominant estrogen in the placenta and excreta during advanced pregnancy but whether it is a secretion of the placenta or a degradation product of estrone is not known. It is suggested that estriol is primarily a primate hormone of pregnancy and may be secreted as such by the placenta. If this be true, its importance in the maintenance of the normal pregnancy can be realized.

J. EDWARD HALL, M.D.

Klinefelter and Jones: Amenorrhea Due to Polycystic Ovaries, p. 1247.

Two cases of the Stein-Leventhal syndrome are presented and discussed. The syndrome is briefly but clearly described and present-day thoughts about it are crystallized. Wedge resection of the ovaries is advocated as the treatment of choice but only after careful and complete work-up to be sure of the diagnosis. The use of cortisone in some cases of adrenal cortex disturbance is described.

J. EDWARD HALL, M.D.

Correspondence

Further Discussion on the Cervical Musculature

To the Editors:

We wish to comment on Danforth's paper entitled "The Distribution and Functional Activity of the Cervical Musculature" (AM. J. OBST. & GYNEC. **68**: 1261, 1954) since he accuses one of us (W. C. W. N.) of being illogical.

He writes that "the cervix was found to be fundamentally a fibrous-tissue structure." In common with other workers, among them Karlson[1] and Woodbury,[2] we have found that the human cervix can contract rhythmically. In 1951, Schild, Fitzpatrick, and Nixon[3] published a paper entitled "Activity of the Human Cervix and Corpus Uteri—Their Response to Drugs in Early Pregnancy."

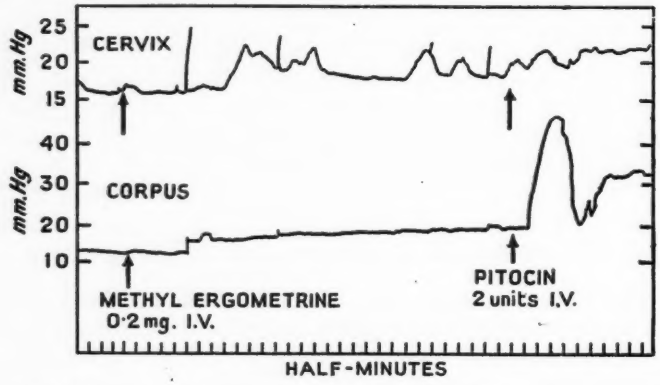

Fig. 1.—At 22 weeks, intravenous methylergometrine (0.2 mg.) causes contractions of the cervix only, whereas intravenous oxytocin (Pitocin, 2 units) causes contractions of the corpus.

In Fig. 1 is a record taken from this paper which shows that contractions in the cervix were not transmitted from the corpus since they occurred in complete absence of pressure changes in the corpus. The intensity of these contractions was fairly considerable with pressure changes of 10 cm. of water.

This record also shows that drugs may have a differential action on the corpus and cervix uteri. In this instance, 0.2 mg. methylergometrine (Methergine) produces a contraction of the cervix without any corresponding effect on the corpus, whereas 2 units of oxytocin (Pitocin) stimulates the corpus with little effect on the cervix.

The strong response of the lower part of the uterus to drugs of the ergonovine series may be the explanation for the placenta's being trapped sometimes in the lower part of the uterus when ergonovine is injected at the time of the birth of the baby's head.

W. C. W. NIXON
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JAN. 19, 1955

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1. Karlson, S.: Acta obst. et gynec. scandinav. 33: 253, 1954.
2. Woodbury, R. A., Torpin, R. Child, G. P., Watson, H., and Jarboe, M.: J. A. M. A. 134:
3. Schild, H. O., Fitzpatrick, R. J., and Nixon, W. C. W.: Lancet 1: 250, 1951.

Reply by Dr. Danforth

To the Editors:

I do not consider my own findings to be necessarily incompatible with those recorded by Professor Nixon. My original paper described the presence of muscle fibers scattered at random throughout the substance of the cervix. The paper to which Nixon refers described in addition the presence of "muscle tissue at the peripheral aspects of the (supravaginal) cervix" to which my original paper made no reference. I agree that this muscle tissue is capable of contracting, and in fact have confirmed this by in vitro studies made in the pregnant uterus, and published in the second paper.

Accordingly, our difference of opinion concerns not whether the cervix can in fact contract, but rather whether it is reasonable to consider this contractile ability as negligible and of minor importance, or whether, as Nixon apparently contends, it is of specific and fundamental importance to proper cervical function.

On the basis of the material which I have studied, it seems inescapable that, although muscle tissue is present in the cervix, its contractile possibilities are negligible when compared with those of the corporeal musculature above. The overwhelmingly predominant quantities of collagenous tissue in the cervix provide a ready explanation for (a) the failure of the cervix to hypertrophy in pregnancy in comparison to the enormous growth of the corpus even though they are exposed in like manner to similar hormones, and (b) the importance of the cervix in preventing loss of the conceptus toward mid-gestation, when the factor of distention enters as a stimulant to uterine growth.

D. N. Danforth

636 Church Street
Evanston, Ill.
April 10, 1955.

Agreement and Disagreement With Danforth's Conclusions

To the Editors:

In your Journal of November, 1954, Dr. Danforth comments on my paper on the structure of the cervix. He makes one point of substance and several debatable points.

The main issue is technical, namely, fixation and staining. At the time I did not mention, in an already long article, details so commonplace as to be assumed. My nonpregnant uteri were opened and immersed in fixative, either promptly after removal, or with varying delays up to six hours. Formalin was used for the sake of uniformity with material from outside sources, and the sections post-chromed.

Danforth has not touched the really pertinent question of how the procedure objected to is connected with the result disagreed with. Now the principal and well-known disadvantage of poor, uncorrected, formalin fixation with these stains is that one tends to lose the red from the muscle, etc., and get overrun by the blue or green counterstain. In a bad cervix of this type, therefore, one would be bound to reach the conclusion, if guided solely by the colour scheme, that the only structure present was collagen. This is not a veiled hint that Danforth's results were reached by such means: on the contrary the procedure he describes seems optimal for this stain. But it does suggest that his criticisms of me on this score are insufficiently considered and are irrelevant. In fairness I must add that in very dense, badly fixed formalin material a blotchy red staining of collagen may occur, but this is uncommon. I do not think anyone could mistake it for muscle and I am sure that I did not.

Danforth makes some play with the fact that one of my specimens, showing a taken-up cervix, is dated 1903. However, all my specimens came from the period 1948-1951, except for three, together with three prepubertal cervices, which came from some unpublished work of Nixon's of the 1930's.

Clearly our attitudes to histological technique are quite different. Mine, which is without piety, regards these special stains, not as pure colour tests, but as accessory aids to identifications, the main burden of which is still largely morphological.

Danforth has misrepresented me on the issue of the distortion of cervical structure in hysterectomy material. His only relevant comment on this perfectly real point is the inadequate one that total hysterectomy removes the whole uterus. Instead he diverts the discussion to the subsidiary question of the fraying of the anterior edge of the muscle by separation of the bladder.

Fig. 1.—Wertheim cervix, from 55-year-old patient, halfway up canal. Left to right, dark rim of radium necrosis, inner two-thirds to three-fourths mainly of collagen, and outer zone of mature muscle with interlaced broad collagen septa. (Carmoisine stain. ×7.)

After this divergence on technical issues it must surely surprise the detached reader to discover, from Danforth's penultimate paragraph, how great is our agreement. I think we are agreed that the cervix is mainly collagen, and that it contains functional muscle at its periphery, which in pregnancy can influence cervical diameter. Danforth thinks that here we "diverge sharply"; he describes this layer as "extremely loose" and "very attenuate," whilst I describe it as "separated by broad septa of loose collagen," obviously the same observation in different words. He implies that I may have been misled by tangential cutting: I do not think so. I think it better to produce a photograph showing an average specimen of this layer (whose thickness varies). If Danforth thinks this picture does significant violence to the average state of affairs, then I suggest he publish a rival photograph, obtained possibly by photographing his red and green stain through a green filter. His objections on this score seem to me rather vague. Surely a photograph is a histologist's only objective testimony whereby he can give the reader a chance to judge for himself.

I hope, however, that our agreement is great enough to make this unnecessary, and perhaps even to eliminate further discussion of this muscle; for I think it is in danger of hiding more vital issues. Neither of us thinks that its local contraction is likely to be of much obstetrical importance, though it seems the most likely compressor of balloons, etc., introduced into the cervical canal. It should not be forgotten also that it is the function of muscle (as opposed to muscle cells) to transmit as well as to produce force, which it does through its organised collagenous framework. The fact that the pull of the upper segment may be partly transmitted down the side of the cervix may well be of obstetrical importance, as my paper suggests. But if the force retaining the ovum and later resisting cervical dilatation is muscular (or partly so), it is almost certainly not this muscle but that around the internal os (called by me "upper cervical muscle") which is important. I therefore freely confess to having confused the issue here in my remarks about Danforth. The fact remains, however, that in his 1947 article he does suggest that his findings show that the force retaining the ovum cannot be muscular.

Danforth misquotes the phrase "distinct submucous layer in which the muscle content is unusually high." By omitting certain phrases, he converts into its opposite an intention to warn the reader not to take the high submucous muscle content of this figure as typical.

I would like to say that though references made to Danforth's work may have been pointed there has been no intention to derogate it; on the contrary I both agree with, and wish to give due credit for, his main finding.

P. E. HUGHESDON

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JAN. 19, 1955

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Danforth, D. N.: AM. J. OBST. & GYNEC. 68: 1261, 1954.
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Lillie, R. D.: Histopathologic Technic, Philadelphia, 1948, The Blakiston Company.

Dr. Danforth's Answer

To the Editors:

Before commenting on Mr. Hughesdon's letter, I should like to acknowledge the work of Ricci, Lisa, Thom, and Kron[1, 2] which has not been cited previously in connection with this discussion. These workers found the cervix to be collagenous, and in their preparations the vaginal musculature was found to become lost in the "dense fibro-elastic tissue of the cervix."

1. The 1949 reference which my paper quoted was in error. The reference should have read "Proceedings of the Royal Society of Medicine, Volume 44, page 871, 1951," a preliminary paper which did have to do with the cervix. Also, his reference to the "distinct submucous layer" quotation from his page 765 is correct. His statement that this error converts the phrase into its opposite is not correct. He has already made the observation that the layer is distinct and readily demonstrable.

2. I cannot think it necessary to emphasize further the desirability of proper fixation of tissue for *any* histological work. I concur that the distinction of fibrous tissue from smooth muscle requires something more than color contrast; but I confess my inability to decide, in autolyzed or improperly fixed tissue, "the true state of affairs from the characteristic form and arrangement of the muscle cells," or to make due allowance for this artifact.

3. The contention that I misrepresented Hughesdon on the issue of distortion in hysterectomy material is not well taken. He states (page 770) that "it seems probable that Danforth, by confining his attentions to hysterectomy material, was misled by the artifact

described earlier [page 765].'' On page 765: ''the extrinsic muscle layer . . . is apt to be obscured by postvital retraction in uteri removed by . . . hysterectomy . . . in an anterior section the muscle gets frayed by the pulling out of connective tissue fibers during dissection of the bladder." I am unable to follow the remainder of Hughesdon's reference to this alleged misrepresentation, and accordingly offer no rebuttal.

Hughesdon has collected certain data concerning the cervix, from which he makes a forthright and positive conclusion. I have collected another set of data, from which I, too, have reached a positive, and equally forthright conclusion. Each of us finds the techniques of examination employed by the other to be objectionable in one or more respects. Hughesdon states that we have recorded "the same observation in different words," and suggests that much of our disagreement is merely a bandying of descriptive terms; since my own concept is set forth as precisely as it is possible for me to do, and since I wish to abide by that description, I am entirely content to leave the matter here.

D. N. DANFORTH

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EVANSTON, ILL.
April 10, 1955

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2. Ricci, J. V., Lisa, J. R., Thom, C. H., and Kron, W. L.: Am. J. Surg. **77**: 547, 1949.

Items

American Board of Obstetrics and Gynecology

The following candidates were certified by the American Board of Obstetrics and Gynecology on May 20, 1955, at the Edgewater Beach Hotel in Chicago, Illinois:

Achilles, William E., Jr.	12 Park Place	Geneva, N. Y.
Ainslie, William H.	73 Amboy Ave.	Metuchen, N. J.
Aldisert, Caesar O.	Schenley Apts.	Pittsburgh 13, Pa.
Alinovi, Victor	117 Newbridge Rd.	Hicksville, N. Y.
Alvis, Walter P.	1791 Howard St.	Chicago, Ill.
Anderson, Clarence L.	910 Broderick Bldg.	Lakeland, Fla.
Anderson, Joseph D.	104 20th Ave., N.	Nashville 4, Tenn.
Angelides, John D.	947 W. 8th St.	Los Angeles 17, Calif.
Arey, John V.	2274th USAF Inf.	Wolters Air Force Base, Tex.
Arrington, Robert G.	1436 Terrace Dr.	Huntington, W. Va.
Atkins, John H.	13944 Euclid Ave.	Cleveland, Ohio
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Bass, Ross F.	514 Woodrow Wilson Ave.	Jackson 3, Miss.
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Beinke, Victor H.	1025 S. 7th St.	Springfield, Ill.
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Berry, Francis X.	823 N. Elm St.	Greensboro, N. C.
Bivens, Melvin D.	4800 Gibson Blvd., S. E.	Albuquerque, N. M.
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Blanton, George C.	718 Alabama Ave.	Selma, Ala.
Bonebrake, MacDonald	609 Cherry	Springfield, Mo.
Boyle, John B.	1226 St. Paul Street	Baltimore, Md.
Brackett, Morris E.	U. S. Army Hospital	Fort Knox, Ky.
Brandeberry, Keith R.	The Holzer Clinic	Gallipolis, Ohio
Brandsted, Ernest C.	823 N. Main St.	McPherson, Kansas
Brenner, Angus L.	1134 Wheatsheaf Lane	Abington, Pa.
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Buell, William O.	860 Fifth Ave.	New York 21, N. Y.
Bulian, Max J.	375 Commonwealth Ave.	Boston 16, Mass.
Bunce, James M.	85 Jefferson St.	Hartford 14, Conn.
Burnett, Lawrence F.	386 Roseville Ave.	Newark 7, N. J.
Burrus, Swan, Jr.	692 W. Forrest	Jackson, Tenn.
Buxton, Bertram H., Jr.	167 Angell St.	Providence 6, R. I.
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Calvelli, George J., Jr.	155 W. Merrick Rd.	Freeport, N. Y.
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Carrabba, Salvatore R.	179 Allyn	Hartford 3, Conn.
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Cohen, Harold R.	303 Evergreen Dr.	Vancouver, Wash.
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Colmer, William M., Jr.	1750 N. Palafox St.	Pensacola, Fla.
Colwell, Leslie C.	1110 Nueces St.	Austin 1, Texas
Commette, Joseph P.	One Monument Square (Single certification in *Obstetrics* only)	Beverly, Mass.
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Covell, James E.	753 James St.	Syracuse, N. Y.
Crenshaw, John L., Jr.	115 E. S. Temple	Salt Lake City, Utah
Crispin, Maximilian A.	350 Farmington Ave.	Hartford 5, Conn.
Crockett, Emily Ethelene J.	7263 American Ave.	Detroit 10, Mich.
Crouch, William L.	807 E. Manship St.	Jackson, Miss.
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Diaz-Carazo, Jose	654 Ponce de Leon Ave.	San Juan, Puerto Rico
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Dobrzynski, Francis A.	258 North St.	Rochester 5, N. Y.
Dorsen, Robert B. G.	U. S. Public Health Service Hospital	Staten Island, N. Y.
Dove, Frederick D., Jr.	214 N. Potomac St.	Hagerstown, Md.
Earnhardt, H. Lee, Jr.	1101 Caroline St.	Fredericksburg, Va.
Eckhous, Arthur W.	1015 Kales Bldg.	Detroit 26, Mich.
Ehrlich, Daniel	11 W. Biddle St.	Baltimore 1, Md.
Ekroth, Richard D.	2nd Field Hospital, Munich, Germany, APO 108, c/o P. M.	New York, N. Y.
Ellis, Francis J.	609 Cherry St.	Springfield, Mo.
Eskridge, James B., III	1220 N. Walker	Oklahoma City, Okla.
Evans, Gerard E.	33 Eighth Ave.	Brooklyn 17, N. Y.
Falco, Paul R.	27 Germania Pl.	Brooklyn 10, N. Y.
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Feldman, Robert L.	1235 Park Ave.	New York, N. Y.
Ferris, George N.	16745 Oakfield	Detroit 35, Mich.
Fielding, Waldo L.	314 Commonwealth Ave.	Boston, Mass.
Fitz Gerald, James L., Jr.	130 N. 14th St.	Allentown, Pa.
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Flynn, Richard T., Jr.	3333 S. 27th St.	Milwaukee 15, Wis.
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Fuller, Harold W.	1220 Central Ave.	Great Falls, Mont.
Gambrel, Francis J.	275 W. Federal St.	Youngstown, Ohio
Gentry, William D., Jr.	Cambridge Arms Apts., Charles and 34th Sts.	Baltimore 18, Md.
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Gittings, Paul E.	5230 Center Ave.	Pittsburgh 32, Pa.
Gordon, Calvin M.	211 Angell St.	Providence 6, R. I.
Gordon, Robert E.	32 Remsen St.	Brooklyn 1, N. Y.
Graceffo, Frank A.	9 William St.	Auburn, N. Y.
Grant, Arthur B.	211 Ninth St.	Racine, Wis.
Gray, James C.	14 Logan Circle, N. W.	Washington, D. C.
Hammond, Daniel O.	350 N. E. 15th St.	Miami 32, Fla.
Hansen, Hodson A.	820 Sharp Bldg.	Lincoln, Neb.
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Hardy, Erving D.	44 West St.	Worcester, Mass.
Hargreaves, William J.	327 Vine St.	Johnstown, Pa.
Harris, James H.	U. S. Naval Hospital	Bremerton, Wash.
Harrod, John P., Jr.	5841 Maryland Ave.	Chicago 37, Ill.

Hayden, Glen E.	Chicago Lying-in Hospital, 5841 S. Maryland Ave.	Chicago 37, Ill.
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Herbert, Joseph W.	6815 Southern Ave.	Shreveport, La.
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Hutchinson, Harry F.	1930 Corlies Ave.	Neptune, N. J.
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Jackson, Haynes G.	301-304 Medical Arts Bldg.	Hot Springs, Ark.
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James, John A.	112 Summer St.	Auburn, Maine
James, Melvin E.	957 Delaware Ave.	Buffalo 9, N. Y.
Jaynes, Richard V.	25300 Fenkell	Detroit 23, Mich.
Jenkins, James H.	2625 S. Irving St.	Denver, Colo.
Johnson, Walter R.	Guthrie Bldg.	Paducah, Ky.
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Kaften, Sheldon H.	47 E. 61st St.	New York 21, N. Y.
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Kaknes, George B.	42 Pleasant St.	Woburn, Mass.
Kane, William M.	6910 Market St.	Upper Darby, Pa.
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Kephart, Stewart B.	303 S. Main St.	Bluffton, Ind.
Kettering, Harry A.	1024 Summit	Seattle 4, Wash.
Keyser, Morton	2000 Washington	Wilmington 2, Del.
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Larkin, Michael J.	705 Hamilton Ave.	Trenton 9, N. J.
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Lawler, Frank C.	1150 W. 78th St.	Chicago, Ill.
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Lebamoff, Alexander T.	6586 Allen Rd.	Allen Park, Mich.
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Leone, Louis B.	8401 N. Crawford Ave.	Skokie, Ill.
Lippsett, Herbert L.	1250 Ocean Ave.	Brooklyn 30, N. Y.
Lloyd, Frank P.	2229 Northwestern Ave.	Indianapolis, Ind.

Loizeaux, Theodore	212 E. 7th St.	Plainfield, N. J.
Long, Frank H., Jr.	412 Linwood Ave.	Buffalo, N. Y.
Long, John S.	720 N. Michigan Avenue	Chicago, Ill.
Longwell, Robert H.	141 E. Lemon St.	Lancaster, Pa.
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McCann, John B.	328 Washington St.	Wellesley Hills, Mass.
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Merritt, Charles W.	1007 S. Oakwood	Beckley, W. Va.
Mighell, Joseph R.	1302 Government St.	Mobile, Ala.
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Miller, Henry W.	627 W. Chestnut St.	Lancaster, Pa.
Miller, Richard L.	330 South St.	Waterloo, Iowa
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O'Brien, John G.	39 Gifford Ave.	Jersey City, N. J.
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Ostreich, Leonard L.	660 Hickory St.	Westbury, N. Y.
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Pepe, Vincent	213 E. Main St.	Meriden, Conn.
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Simpson, James L.	311 Pendleton	Rock Hill, S. C.
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Sinsky, John E.	335 W. North Ave.	Milwaukee 12, Wis.
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Stevenson, Lee B.	16 S. Henry St.	Madison 3, Wis.
Stone, Raymond E.	Medical Arts Bldg.	Princeton, N. J.
Stouffer, James G.	1506 W. Terrell St.	Ft. Worth 4, Texas
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Wohl, Zachary	1322 Aline	New Orleans 15, La.
Wolters, Carlton E.	1207 Hermann Professional Bldg.	Houston, Texas
Woolf, Ralph B.	630 S. Kingshighway	St. Louis 10, Mo.
Wright, Charles H.	1549 W. Grand Blvd.	Detroit, Mich.
Zaneski, Bruno W.	496 Jefferson St.	Westbury, L. I., N. Y.
Ziel, Hermann A., Jr.	1101 N. Eighth St.	Sheboygan, Wis.

International Fertility Association

The Second World Congress of the International Fertility Association will be held in Naples, May 18 to 26, 1956.

For further information write to Prof. G. Tesauro, S. Andrea delle Dame, 19, Naples, Italy.

Canadian Society for the Study of Fertility

The second annual meeting of the Canadian Society for the Study of Fertility will be held in Toronto, Oct. 6 to 8, 1955, at the Royal York Hotel.

For further information write to Dr. Earl R. Plunkett, Secretary Treasurer, 469 Waterloo Street, London, Ontario, Canada.